DISSERTATION ON

PAEDIATRIC OPTIC NEURITIS: CLINICAL PROFILE AND VISUAL OUTCOME

Submitted in partial fulfillment of the requirements of

M.S.OPHTHALMOLOGY
BRANCH III

REGIONAL INSTITUTE OF OPHTHALMOLOGY AND GOVERNMENT OPHTHALMIC HOSPITAL (RIO-GOH) & MADRAS M E D I C A L COLLEGE (MMC)
EGMORE, CHENNAI

THE TAMIL NADU DR.M.G.R.MEDICAL UNIVERSITY, CHENNAI

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CERTIFICATE

Certified that this dissertation titled **"PAEDIATRIC OPTIC NEURITIS: CLINICAL PROFILE AND VISUAL OUTCOME"** is a bonafide record of research work done independently by **Dr. B. Sahithya,** post graduate in Regional Institute of Ophthalmology & Government Ophthalmic Hospital, Madras Medical College and Research Institute, Chennai-03, submitted in partial fulfillment of the regulations laid down by the Tamil Nadu Dr.M.G.R. Medical University, Chennai for the award of M.S.Ophthalmology Branch III, under my guidance and supervision and that it has not previously formed the basis for the award of any degree, fellowship or associateship to her.

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DECLARATION

I hereby declare that this dissertation titled "PAEDIATRIC OPTIC NEURITIS: CLINICAL PROFILE AND VISUAL OUTCOME" is a bona fide record of research work done by me during the course of research under the guidance of Prof.Dr.K.NamithaBhuvaneswari, M.S.,D.O. and that the thesis has not previously formed the basis for the award to me of any degree, diploma, associateship, fellowship or other similar title, of any other university or society

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Date:

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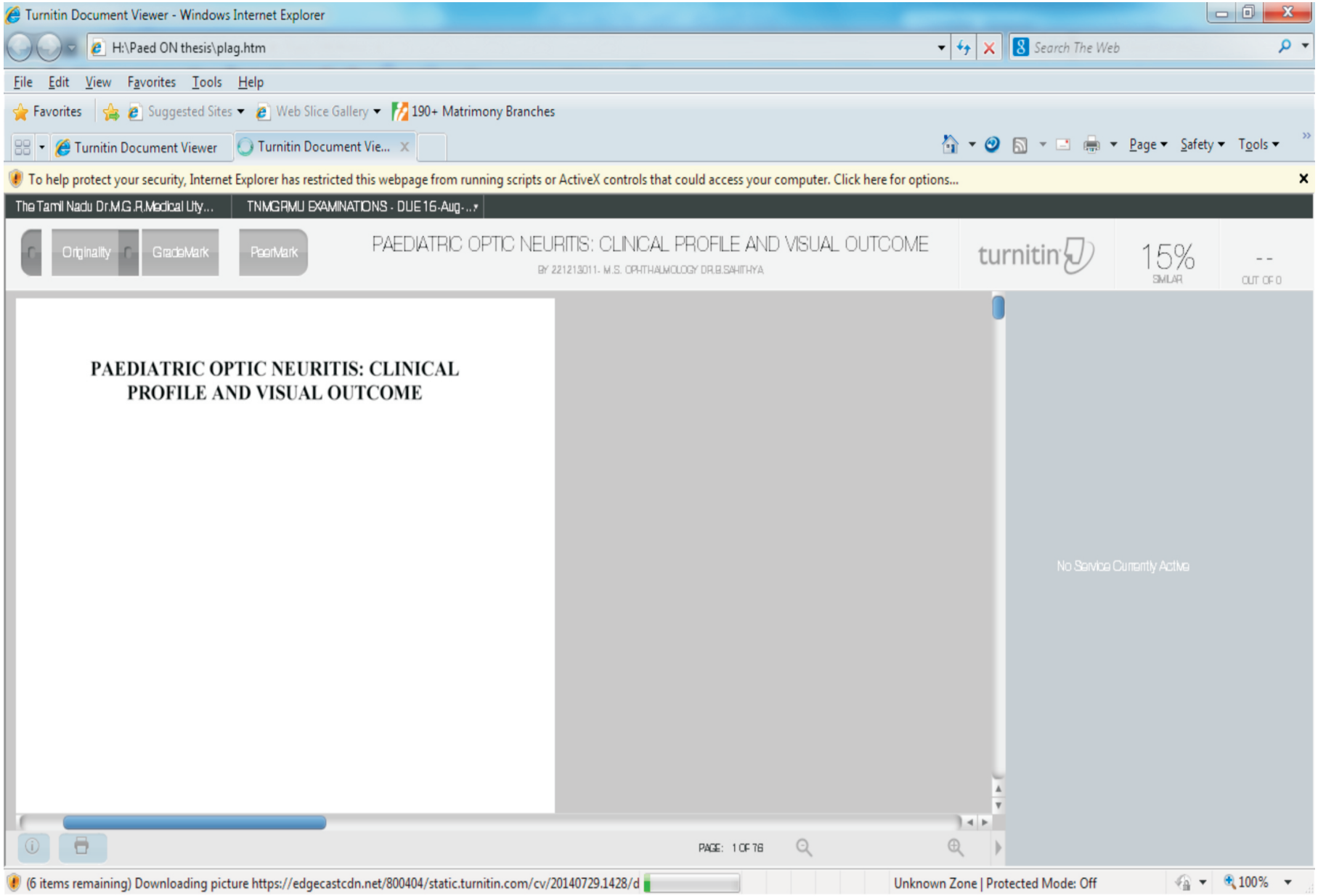
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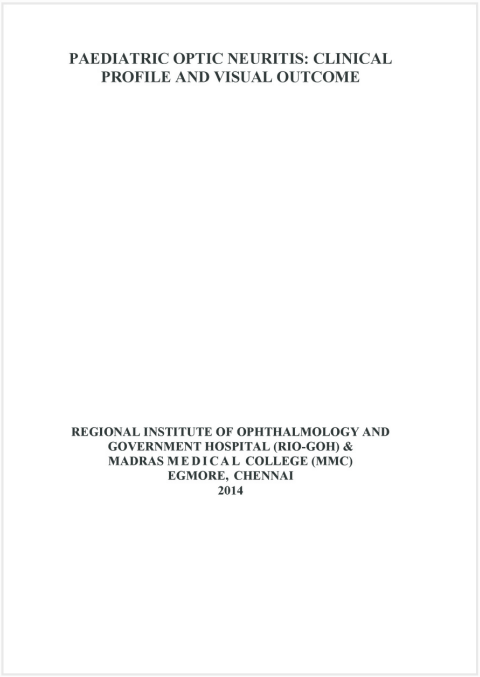

PAEDIATRIC OPTIC NEURITIS: CLINICAL PROFILE AND VISUAL OUTCOME

REGIONAL INSTITUTE OF OPHTHALMOLOGY AND GOVERNMENT HOSPITAL (RIO-GOH) & MADRAS MEDICAL COLLEGE (MMC) EGMORE, CHENNAI 2014

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CONTENTS

ABBREIVATIONS

ADEM	-	Acute Demyelinating Encephalomyelitis
M S	-	Multiple Sclerosis
ONTT	-	Optic Neuritis Treatment Trial
RAPD	-	Relative Afferent Pupillary Defect
MRI	-	Magnetic Resonance Imaging
CSF	-	Cerebrospinal Fluid
VEP	-	Visual Evoked Potential
VER	-	Visual Evoked Response
MBP	-	Myelin Basic Protein
IFN	-	Interferon
HLA	-	Human Leucocyte Antigen

PART - I

INTRODUCTION

Optic neuritis is a multi-etiological condition consisting of inflammation of the optic nerve that may cause a complete or partial loss of vision. The optic nerve comprises axons that emerge from the retina of the eye and carry visual information to the primary visual nuclei, most of which is relayed to the occipital cortex of the brain to be processed into vision. Inflammation of the optic nerve causes loss of vision usually because of the swelling and destruction of the myelin sheath covering the optic nerve. Direct axonal damage may also play a role in nerve destruction in many cases.

Optic neuritis affects young adults ranging from 18-45 years of age with a mean age of 30-35 years with a strong female predominance. The annual incidence is approximately 5/100000 with a prevalence of 115/100000

The most common etiology is Multiple Sclerosis (MS). Up to 50% of patients with MS will develop an episode of optic neuritis and 20-30% of the optic neuritis is the presenting sign of MS. Some other causes of optic neuritis include infection (e.g. syphilis, Lyme disease, herpes zoster), autoimmune disorders (e.g. lupus, neurosarcoidosis), inflammatory bowel disease, drug induced (e.g. chloramphenicol, ethambutol), vasculitis, B12 deficiency and diabetes.

The incidence of optic neuritis is more among the populations located at higher latitudes, in the northern United States and Western Europe and is less in regions close to the equator. In United States, studies have estimated the annual incidence of optic neuritis was as high as 6.4 per 100000 (Percy et.al. 1972 and Rodriguez et.al. 1995). In the United States, optic neuritis occurs more frequently in whites than black (Phillips et.al.1998) In Asia, optic neuritis is proportionately more common related to the incidence of multiple sclerosis than in the United States or Western Europe (Wakakura et.al.1999).

It is an inflammatory disorder of the optic nerve often presenting with periorbital pain, decreased visual acuity and decreased colour vision. Differential diagnoses include various infectious and autoimmune disorders. Demyelinating optic neuritis can present as isolated optic neuritis with no lesions elsewhere in the central nervous system or can be associated with acute disseminated encephalomyelitis, multiple sclerosis or neuromyelitis optica. The subsequent diagnosis of multiple sclerosis is reported in 19-42 per cent of children with optic neuritis.

Clinically, optic neuritis in the pediatric age group is diagnosed by the same criteria used in adults including sudden or sub acute visual loss, central or cecocentral visual field defect, impairment of colour vision, afferent pupillary defect and ocular pain on eye movements.

Paediatric Optic Neuritis is a rare condition which differs from adult onset optic neuritis in clinical and evaluative aspects. It frequently presents at 7 years of age, more commonly in girls than in boys, usually bilateral, although frequently asymmetric and it is often associated with a febrile illness. It carries a good prognosis and a relatively low risk of developing subsequent neurologic disease (Multiple Sclerosis). On the contrary, optic neuritis in adults is usually unilateral, predominantly affects the retrobulbar portion of the optic nerve and presents a high conversion rate to Multiple Sclerosis. In contrast to adult optic neuritis, pattern evoked potentials in pediatric optic neuritis though abnormal at presentation, become normal at follow up, suggesting the benign nature of this condition in children.

At presentation, children have profound central visual loss, loss of colour vision, a central scotoma, and afferent pupil defect with optic disc swelling and few retinal hemorrhages. Despite the severity of visual loss and optic disc pallor, most children recover good visual acuity. The restoration of normal visual evoked potential latency in children substantiates the possibility of remyelination that is more rapid and efficient in children. Although it has been established that intravenous methylprednisolone speeds the recovery of optic neuritis, the ultimate effect of intravenous steroids is unknown.

Nevertheless, the dramatic recovery shown by patients precludes surgeons to withhold treatment especially in bilaterally affected cases.

Though these facts are accepted on a worldwide basis, there are very few series publicised on childhood optic neuritis especially in Indian population.

The present study is undertaken to evaluate the clinical characteristics, neuroimaging findings, efficacy of intravenous steroid, and visual outcome in pediatric optic neuritis.

ANATOMY

The optic nerve being the second cranial nerve is a white matter tract of the brain. The optic nerve does not regenerate once severed. The optic nerve extends from the optic nerve head in the eye to the anterior part of chiasma. Its length ranges from 3.5 cm to 5.5 cm for an average adult. It is comparatively shorter in children. It is sub-divided as four parts namely :

1. Intraocular (0.7mm) – shortest part
2. Intraorbital (3.0cm) – Longest part
3. Intra canalicular (6mm to 1.0 cm)
4. Intracranial (1.0cm)

Optic nerve head is the visible portion of the intraocular portion of the optic nerve. The optic nerve head is around 1.5mm in width. The intraocular part is further divided as prelaminar and retro-laminar segments. The intraocular part passes backward through the sclera bridged by lamina cribrosa, a sieve like structure. The fibres of the optic nerve pass through these sieve like openings. The optic nerve anterior to lamina cribrosa is not myelinated and myelination of the nerve begins behind the lamina cribrosa.

Intra orbital part is the longest segment of the optic nerve. It is bent downward anteriorly and medially in its posterior part. This is a protective mechanism against stretching of the nerve. The intraorbital part lies intraconally surrounded by orbital fat. Through its course here, it is surrounded by dura, aracnoid and pia mater. The central retinal artery and central retinal vein pass through the subararachnoid space in to the optic nerve from below, around 10 – 12 mm behind the globe.

At the apex of the orbit , the nerve is surrounded by annulus of zinn which id the origin of recti muscles. The superior rectus and medial rectus at their origin are closely attached to the optic nerve dural sheath. In inflammation of optic nerve, stretching of this attachment causes pain on extraocluar movements. The ciliary ganglion lies lateral to optic nerve. The lower division of occulomotor, abducent, sympathetic fibres, nasociliary nerve lie between lateral rectus and optic nerve. Ophthalmic artery crosses above the optic nerve in its posterior part.

The intracanalicular part is protected in the bony canal along with meninges, ophthalmic artery, sympathetic fibres and is not mobile. The intracranial part is situated in the middle cranial fossa extending from optic canal to anterolateral angle of optic chiasma.

BLOOD SUPPLY OF OPTIC NERVE :

(Fig.1)

The main blood supply of the optic nerve is derived from

1. Internal carotid and its branches
2. Anterior cerebral artery

Blood supply to optic nerve head is derived from

Retinal and Ciliary vessels

The surface of the optic nerve is supplied by branches of central retinal artery that anastamoses with branches of the prelaminar portion.

The prelaminar and laminar portion of the optic nerve are supplied by short posterior ciliary artery. Retrolaminar part of the optic nerve is supplied by both retinal and ciliary circulation.

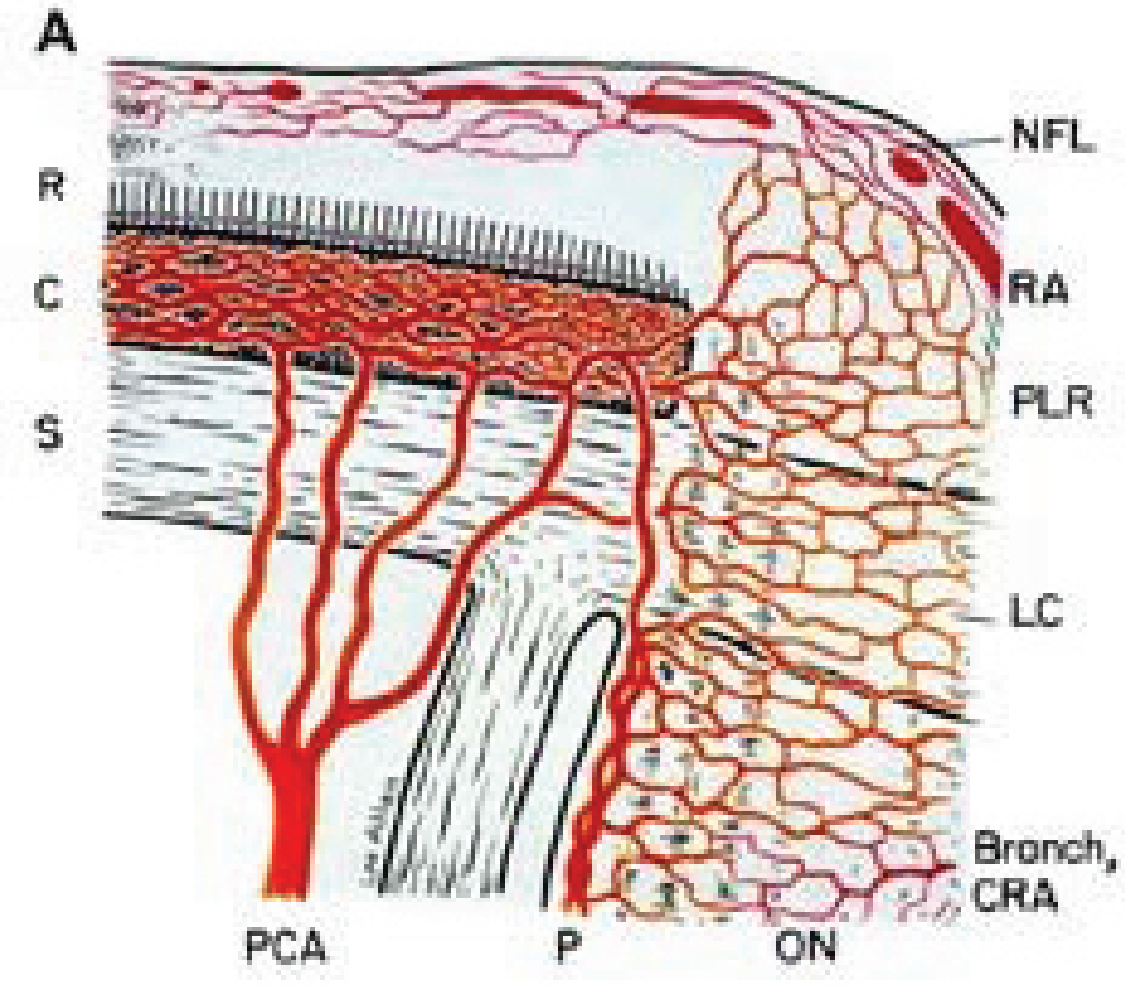


Fig.1. Blood supply of optic nerve

DEVELOPMENT OF OPTIC NERVE

The precursor of the optic nerve is the optic stalk which joins the forebrain and the eye. The embryonic fissure which develops at the lower side of the optic cup extends in to the optic stalk. At its underside the optic stalk elongate with a groove. At the end of six weeks, the fibres from the optic cup grow in to the optic stalk. At six weeks, the hyaloids artery enters the optic nerve. Small capillaries develop in the optic nerve by the third month of gestation. The meninges covering the optic nerve namely pia, dura and arachnoid mater are well defined by seven months of gestation. The lamina cribrosa develops partly from sclera and partly from choroid. As the axons of ganglion cells grow in to the developing optic nerve, a few retinal cells isolate from the main body and separately clump together to form the early optic nerve head. At birth, the elevated area and forms the optic cup. Optic nerve myelinates late and starts first in the lateral geniculate body and proceeds to the eye. Myelination is complete at birth and stops short behind the lamina.

Pathogenesis of Optic Neuritis

Demyelination

Almost half of Multiple sclerosis patients have clinical evidence of a having had optic neuritis in the past (at autopsy, almost 100% have optic neuritis), and 20% of these patients present with optic neuritis as their first sign . The initial event before demyelination is the inflammation of the vascular endothelium leading to breakdown of the blood-brain barrier.

The lack of oligodendrocytes in the retina lead to perivenular. This venous sheathing represents a clinically silent retinal disease preceeding the development of optic neuritis. This finding may not be apparent on opthalmoscopic examination but may show up on fundus fluorescein angiography. The underlying defect in optic neuritis or multiple sclerosis involves demyelination of the optic nerve leading to a blocked or slow conduction of axonal transmission or a decrease in amplitude of the action potential of the optic nerve. Varying degrees of loss of vision may result from this process.The perivenular demyelinating plaques of optic nerves of patients who have acute MS show similar pathology to the periventricular plaques

found elsewhere in the brain. These plaques show a perivascular cuffing of lymphocytes, edema of myelin nerve sheaths, and subsequent myelin breakdown. Usually in optic neuritis the axons of the optic nerve are spared, resulting in good visual recovery. Advanced lesions elsewhere in the white matter of brain often involve axonal degeneration, resulting in physical or mental disability. On histopathology, macrophages engulf the degraded debris of myelin products and glial cells proliferate to cause permanent conduction block resulting in no clinical recovery.

Cell-Mediated Damage

Cellmediated cytotoxicity is one of the neuroimmunological factors that mediate demyelination of the optic nerve involve . Studies claim that 76% of the patients who had optic neuritis were found to have encephalitogenic, myelin basic protein(MBP), cerebroside, and ganglioside antibodies. Patients with optic neuritis/MS and patients who had isolated optic neuritis with cerebrospinal fluid (CSF) oligoclonal bands had encephalitogenic antibodies.

Elevated T-cell-mediated cytotoxicity against the encephalitogenic peptide is highly specific marker for demyelination in MS. Optic neuritis patients who turn out to be positive for this antigen have a higher risk of developing clinically definite MS. The increased CSF MBP- and MBP-reactive B cells in patients with optic neuritis might correlate with the process of early myelin breakdown or its restoration. Although magnetic resonance imaging (MRI) generally has been accepted as a marker of disease activity in MS patients, the concentration of MBP in CSF also has been a useful marker during acute exacerbations in disease activity. It correlates significantly with the visual acuity in patients who have optic neuritis, the Kurtzke expanded disability status scale score in patientswho have MS, the cerebrospinal leukocyte count, intrathecal immunoglobulin G synthesis, and the cerebrospinal albumin concentration quotient. Furthe, the activated T cells recognizing MBP peptides secrete interferon-gamma (IFN-γ). The cytokine profile of interleukin-4, IFN-γ and tumor growth factor-β in patients with optic neuritis was same as that found in patients with CDMS.The production of these cytokines is much higher in the CSF than systemically, which highlights the autonomy of the immune responses in the CSF. The upregulation of these cytokines has been demonstrated in early MS, as manifested by acute optic neuritis associated with more than two MS lesions on MRI brain and CSF oligoclonal IgG bands .

The activated IFN-γ-produced by T cells in the inflammatory foci of optic nerve sections in rats with acute experimental allergic encephalomyelitis showed raised levels of calpain expression.

Calpain has been implicated in the pathogenesis of optic neuritis in multiple sclerosis as it degrades axonal and myelin proteins MBP, neurofilament proteins, and myelin-associated glycoprotein. The proinflammatory cytokines tumor necrosis factor and lymphotoxin in the CSF were found to be high in patients who had optic neuritis to the same degree as patients who had CDMS. Anti-MBP and antimyelin phospholipid protein (PLP) antibodies significantly contributeto the pathophysiology of optic nerve damage. Patients with isolated optic neuritis had significantly more antiPLP-secreting B cells in the blood compared to patients sufferin from neurological diseases; anti-PLP antibodies are more specific for demyelinating disease than is anti-MBP antibody. It is found to be associated with a subtype of MS that has less frequent inflammation in the CSF and CNS parenchyma, whereas anti-MBP antibody is associated with the commoner form of MS, which has frequent prominent inflammatory CSF and CNS features. The increased CNS synthesis of anti-MBP and anti-PLP antibodies is found in patients who have optic neuritis, irrespective of the cause. The synthesis of these antibodies is not associated with the presence of the human leukocyte antigen (HLA)-DRB1 gene.

Genetic Factors

Studies in western literature have shown that first-degree relatives have a 25 to 50 times greater risk of being affected compared to the general population. Overall, the risk is maximum in monozygotic twins, with a concordance rate of about 30% in dizygotic twins and less than 10% in other siblings, thus providing strong evidence for genetic factors in MS. In siblings, the earliest symptoms of the disease tend to cluster by age rather than by year, which suggests that genetic factors influence the onset of the disease. Association studies with casecontrol design, testing specific candidate genes and studying sporadic and familial cases, shows that the only consistently replicated finding has been an association with HLA-DR2 allele within the major histocompatibility complex (MHC) located on chromosome 6. Haines et al. in his study strongly indicated that sporadic and familial MS share a common genetic susceptibility. These studies support the hypothesis that a genetically determined immune response is primarily responsible in the pathogenesis of MS. Furthermore, the MHC locus represents only less than half of the total genetic etiology of MS. Families in whom the HLA-DR2 allele appears to have no linkage to MHC and therefore they are most probably influenced by other genes.

According to the study by The Multiple Sclerosis Genetics Group in 2002,the association of DR2 in families with diverse clinical presentations suggests that there exists a common genetic basis to different clinical phenotypes of MS. The MHC genes primarily influence penetrance, whereas other loci modulate specific phenotypes, such as location in the brain or spinal cord, demyelination, and the severity of inflammation. Epigenetic factors, namely the selection of different disease-inducing antigens, influence the location and severity of experimental allergic encephalitis phenotypes when induced with different encephalitogenic peptides. It is very likely that a similar interplay of genetic and epigenetic factors operate in human MS. The HLA region at 6p21 and various other suggestive loci have been proposed. Therefore, non-HLA genes or other epigenetic factors must also modulate disease expression. Heterogeneity of locus at the HLA region suggests a distinct immunopathogenesis in DR2 negative patients. Different classes of HLA are found to have different roles in susceptibility to MS. The DR2, A23, and B21 allele is associated with the evolution of optic neuritis to CDMS. The high prevalence of A23 and DR2 alleles in CDMS patients when compared with the normal population suggests an important role for these alleles in the development of MS. The B51 allele might be a protective factor against the development of optic neuritis in the general population.

Mitochondrial DNA mutations may also play a role in the causation of MS. Pathogenic mitochondrial DNA point mutations usually are not implicated in typical optic neuritis/MS. Only certain secondary LHON mutations are found to be associated with MS and optic neuritis. This partial overlap between the two conditions may be related to the association of MS with mitochondrial DNA haplotype (a set of mitochondrialDNA polymorphisms) within which LHON mutations preferentially occur.

Epidemiological Factors

Age, sex, and race play some role as risk factors for the development of MS. The onset of optic neuritis in younger age group is a predictive factor in the development of MS. One study reported that the relative risk for MS increases by a factor of 1.7 for each decade less than 54 years of age in adults. There is also a preponderance for females to develop MS after optic neuritis, such that 69% of females and 33% of males developed MS after approximately 15 years following their initial attack of optic neuritis. Based on the 2-year data from the ONTT, Caucasians were at a higher risk than African Americans to develop MS, even after 4 years of follow-up. The geographical location of residence in relationship to the distance from the equator during the first 15

years of life is attributed to be a major risk factor for the development of MS after optic neuritis. Children younger than 15 years of age will acquire the risk of the country to which they migrate. It is not yet certain whether people who migrate later in adulthood retain the risk of their original country or the risk of their new residence. The fall and winter months are also identified as risk factors. One study showed that 43% of 42 patients developed MS with an onset of optic neuritis between October and March; only 29% of 44 patients whose onset of optic neuritis occurred between April and September developed MS.

OPTIC NEURITIS IN CHILDREN

Pediatric optic neuritis usually presents bilaterally with associated headache. Periorbital pain worsening with eye movements supports a diagnosis of optic neuritis. It is most often not related to MS, but is usually associated with a postinfectious or postimmunization etiology. Pediatric optic neuritis is often preceded by a febrile prodromal illness, such as a bacterial or viral infection. Optic neuritis in children is characterised by visual loss, relative afferent papillary defect, abnormal optic disc appearance, visual field defects, and color vision abnormalities. Papillitis is seen in 60% to 70% of children and in only 35% of adults. Both clinical and VEP parameters improve until vision recovers. In a recent 1-year follow-up study of 12 children with optic neuritis (6 with bilateral and 6 with unilateral optic neuritis), 14% of all eyes had residual visual loss , relative afferent papillary defects (67% at onset), visual field defects (58.5% at onset)and 85% had abnormal optic disc appearance;, and color vision defects (56%at onset) resolved a year later. VEP were abnormal in 83% of eyes initially and in 56% at the end of one year. Complete clinical and VEP recovery occurred in 3 children. Visual recovery in the other children was attained within 1 year. Children who present unilaterally have a higher tendency to develop MS. The incidence of MS following unilateral and bilateral childhood optic neuritis has varied from 5.2% to 55.5% in various studies.

Kriss et al. found that MS developed in 3 of 29 (10.3%)children with bilateral optic neuritis and 3 of 10 (30%) children with unilateral optic neuritisover a mean follow-up of 4.6 years. Although children with bilateral optic neuritis have alower incidence of MS than those with unilateral optic neuritis, the risk in those with bilateral optic neuritis cannot be dismissed as negligible. In 8 of the 30 patients from the Kennedy and Carroll series who developed MS over a mean follow up of 8 years, 4 had simultaneous bilateral optic disc swelling. According to Riikonen, MS developed in 7 of 8 (87.5%) patients with unilateral optic neuritis and in only 2 of 15 (15.4%) patients with bilateral optic neuritis over a mean follow-up of 7 years. This study showed that all patients who later developed MS had a second attack of optic neuritis within 1 year of the first attack. Morales et al. found that children who developed MS were, on average, older at presentation with optic neuritis than those who did not develop MS

TREATMENT OF OPTIC NEURITIS

Corticosteroids

Visual recovery is accelerated with the use of intravenous (IV) methylprednisolone within the first 2 to 3 weeks of onset of visual symptoms. In the ONTT, visual acuity improved to 20/25 after 4 days of IV methylprednisolone, compared with 15 days of no therapy or oral steroids. After 1 month, the recovery rate was similar in treated and placebo-oral steroid groups. Most visual recovery is completed by the end of one month. Further improvement may occur 6 months to a year later. The major conclusions of the ONTT trial are related to treatment guidelines in the use of corticosteroids. Treatment with high-dose IV methylprednisolone followed by 2 weeks of oral prednisone accelerated visual recovery but did not give any long-term benefit to final visual outcome. At 6 months, the IV corticosteroid group had better contrast sensitivity and visual color function. One year later, all the groups had similar recovery of the foregoing functions. Conversely, treatment with oral prednisolone alone did not improve the ultimate visual outcome. In fact, it increased the risk of a new attack of optic neuritis in either eye. Within the first 2 years of follow-up in the ONTT, a new attack of optic neuritis occurred in 30% of the oral prednisone group, 16% of the placebo group, and 13% of the IV methylprednisolone group.

Table 1 : A comparison of features of optic neuritis in adults and children

Adult optic neuritis	Pediatric optic neuritis
Unilateral	Bilateral
Usually associated with upon eye movements	Associated with headache
Retrobulbar optic neuritis	Papillitis
Usually idiopathic	Usually postinfectious or Postimmunization
Likely to recur as CNS infl ammatory relapses and to progress to MS	NOT likely to have demyelinating relapses or progress to MS

REVIEW OF LITERATURE

This chapter deals with the review of literature based on the past research work done in the problem of the study. The objectives of the research study necessitated the collection of literature as per the operational objectives framed for the study. The reviews of literatures with reference to the objectives are presented as follows:

Clinical features, neuroimaging, cerebrospinal fluid findings and long term prognosis were reviewed in 26 children diagnosed with optic neuritis at the first presentation of demyeliting disease. The risk factors for the subsequent diagnosis of multiple sclerosis were analysed. The mean duration of follow up was 6-2 years. Six children have been diagnosed with multiple sclerosis (23%)

Acute features: optic neuritis is usually monocular in its clinical presentation. In about 10 percent of cases, symptoms occur in both eyes either simultaneously or in rapid succession (de la Cruz and Kupersmith 2006). Bilateral optic neuritis is more common in children younger than 12 to 15 years old and also in Asian and black South African patients (de la Cruz and Kupersmith 2006 and Wilejto et.al.2001). Because bilateral symptoms are relatively uncommon, they should suggest an alternative cause of optic neuropathy.

However, Rodriguez et.al.1995 and Beck et.al.1993 explained that the subclinical visual deficits in acuity, contrast sensitivity, colour vision and visual field in the contralateral eye can often be elicited by detailed visual testing in patients with clinically monocular disease. Because these deficits usually resolve along with the clinical deficits in the symptomatic eye, it was unlikely that these findings represent prior episodes of optic neuritis.

Other clinical features of optic neuritis were systematically characterized in the Optic Neuritis Treatment Trial (ONTT), which enrolled 457 patients, aged 18 to 46 years with acute unilateral optic neuritis (Optic Neuritis Study Group 1991). The two most common symptoms of optic neuritis were vision loss and eye pain:

Vision loss typically develops over a period of hours to days, peaking within one to two weeks. Continued deterioration after that time suggests an alternative diagnosis (Balcer 2006 and Foroozan et.al.2002). Greater than 90 percent of patients in the ONTT had a significant decrease in central visual acuity. In most, the visual acuities ranged from 20/25 to 20/190 (median visual acuity 20-60). However, some patients had 20/20 acuity (11 percent) and at the other extreme, a few had no light perception (3 percent).

Eye pain occurred in 92 percent of patients in the ONTT and other worsened with eye movement (Optic Neuritis Study Group 1991). The onset of pain generally coincided with the visual acuity loss and improved along with it.

The other common visual symptoms and signs include:

An afferent pupillary defect always occurs in optic neuritis if the other eye was uninvolved and otherwise healthy. This was demonstrated by shining a light alternately in one eye and then the other and finding that the direct response to light was more sluggish in the affected eye. The room should be dark and the patient should fixate on a distant target to prevent miosis due to accommodation.

The visual field defect in optic neuritis was typically characterized as a central scotoma (Balcer, 2006 and Gerling 1998). Visual field defects usually resolve in the ONTT, 56 percent had normalized at one year and 73 percent had normalized at 10 years. (Keltner et.al.1994 and Beck et.al.2004).

Papillitis with hyperemia and swelling of the disk, blurring of disk margins and distended veins was seen in one third of patients with optic neuritis (Optic Neuritis Study Group 1991).Two-third of these patients had retrobulbar neuritis with a normal funduscopic examination. Papillitis was more common in children less than 14 years old and in certain ethnic population including black South Africans and South Asians.

Peripapillary hemorrhages were rare in optic neuritis but were a common accompaniment to papillitis due to anterior ischemic optic neuropathy (Balcer, 2006).

Photopsias (flickering or flashes of light) were often precipitated with eye movement and were reported by 30 percent of patients in the ONTT (Optic Neuritis Study Group 1991).

Loss of colour of vision out of proportion to the loss of visual acuity was specific to optic nerve pathology. Abnormal colour vision by Ishihara plates was found in 88 percent of involved eyes in the ONTT and it further increased to 94 percent with the more sensitive Farnsworth-Munsell 100 hue test (Optic Neuritis Study Group 1991).

Other signs of ocular inflammation may be observed by the ophthalmologist on funduscopic or slit lamp examination. Perivenous sheathing or periphlebitis retinae could be seen in about 12 percent of patients with optic neuritis and implied a high risk for multiple sclerosis (MS) (Rodriguez et.al.2995 and Lightman et.al.1987).

Chronic Signs of optic neuritis can include:

- Persistent visual loss: Most patients with optic neuritis recover functional vision within one year.

  However, on testing, deficits in colour vision, contrast sensitivity, sterio acuity and light brightness were detectable in most patients at up to two years (Brusa et.al.2001).

- A relative afferent pupillary defect remained in approximately one-fourth of patients two years after presentation (Brusa et.al.2001).

- Colour desaturation refers to a qualitative inter– eye difference in colour perception that could be tested by comparing vision of a red object with each eye. A patient with monocular “red desaturation” may report that the red colour appears “washed out”, Pink or orange when viewed with the affected eye.

- Temporary exacerbations of visual problems in patients can occur with increased body temperature (Uhthoff’s phenomenon). Hot showers and exercise are classic precipitants.

- Optic atrophy to at least some degree almost always follows an attack of optic neuritis, despite the return of visual acuity (Cleary et.al.1997). Normal 20/20 visual acuity required less than one-half of normal foveal axons (Miller et.al.2005). The disc appeared shrunken and pale, particularly in its temporal half (temporal pallor).

  The disc pallor extended beyond the margins of the disk into the peripapillary retinal nerve fiber layer.

- The pattern-shift visual evoked response remained delayed in most patients even with visual recovery. Although latencies continue to shorten (improve) up to two years after presentation, abnormalities were seen in most (80 percent) at two years (Brusa et.al. 2001, Hickman et.al. 2004 and Celesia et.al. 1990).

Differential diagnosis:

In a young child, infectious and post infectious causes of optic nerve impairment should be considered as alternatives to optic neuritis, while in an older patient (>50years), ischemic optic neuropathy (for example, due to diabetes mellitus or giant cell arteritis) was more likely diagnosis than optic neuritis.

Diagnosis: In general, optic neuritis is a clinical diagnosis based upon the history and examination findings. Because important findings on funduscopic examination help differentiate typical from atypical cases of optic neuritis, an ophthalmologic examination should be considered an essential feature of the clinical evaluation.

Diagnostic testing was directed towards excluding other causes of visual loss in atypical cases and in assessing the risk of subsequent multiple sclerosis (MS).

Magnetic Resonance Imaging:

A magnetic resonance imaging study (MRI) of the brain and orbits with gadolinium contrast provides confirmation of the diagnosis of acute demyelinating optic neuritis and important prognostic information regarding the risk of developing MS.

Innovations in MRI technology e.g. Short tau inversion recovery (STIR), fast spin echo (FSE), Fluid attenuated min version recovery with fat suppression

technique(FLAIR) and diffusion tensor imaging (DTI) improved imaging of the optic nerve (Barker et.al.2000,Jackson et.al. 1998 and Naismith et.al.2009).Optic nerve inflammation can be demonstrated in about 95 percent of patients with optic neuritis with gadolinium contrast-enhanced

MRI of the brain and orbits (Rizzo et.al.2002, Rocca et.al.2005 and Kupersmith et.al. 2002). The longitudinal extent of nerve involvement as seen on MRI correlated with visual impairment at presentation and with visual prognosis (Hickman et.al.2004, Rizzo, 2002 and Kupersmith et.al.2002). Gadolinium enhancement persists for a mean of 30 days since onset (Hickman et.al.2004).

The signal abnormality in the nerve could still be seen after recovery of vision and was also present in as many as 60 percent of patients with MS who did not have a clinical history of optic neuritis (Hickman et.al.2004, Youl et.al 1996, Miller et.al. 1988 and Davies et.al.1998).

The brain MRI often showed white matter abnormalities characteristic of MS. Typical lesions were ovoid, perventricular and larger than 3 mm. The reported prevalence of white matter abnormalities varies substantially among patients with optic neuritis (23 to 75 percent) (Dalton et.al.2003).

In the ONTT, almost 40 percent of patients had MRI lesions but this trial represents a selected patient group(Optic Neuritis Study Group 1991).Small cases series of unselected patients noted a higher coincidence of MRI brain lesions.(Hickman et.al.2004, Jacobs et.al.1997 and Stadt,et.al.1990). Individuals with white matter abnormalities were at a higher risk of developing MS. The yield of spinal cord imaging is low in unselected patients. Among 115 patients presenting with optic neuritis, MRI abnormalities in the spinal cord were seen in only four patients with a normal brain MRI (Dalton et.al.2003).

Lumbar puncture:

Lumbar puncture is not an essential diagnostic test in optic neuritis but should be considered in atypical cases

(E.g. those with bilateral presentation, <15 years in age or symptoms suggesting infection) (Boomer and Siatkowski, 2003 and Beck and Trobe 1995).

Approximately 60 to 80 percent of patients with acute optic neuritis had nonspecific abnormalities in the cerebrospinal fluid (CSF) including lymphocytes (10 to 100) and elevated protein (Jacob et.al.1997).

Other CSF findings in optic neuritis could include (Nilsson et.al. 2005):

* Myelin basic protein in about 20 per cent

* IgG synthesis in 20 to 36 percent

* Oligoclonal bands (OCB) in 56 to 69 percent.

The presence of OCB implies a higher risk of developing MS. However, since OCB are also associated with white matter lesions on brain MRI, their presence is not clearly of independent prognostic importance.

Other testing:

When there are relevant clues to an alternative diagnosis measurement of the erythrocyte sedimentation rate, antinuclear antibodies and angiotensin converting enzyme levels and serologic and CSF tests for Lyme disease and syphilis should be obtained (Boomer and Siatkowski, 2003 and Beck and Trobe 1995).

Fluorescein angiography was not routinely performed in the evaluation of optic neuritis and was often normal. Up to 25 percent demonstrated either dye leakage or perivenous sheathing (Lightman et.al.1987).These findings may identify patients at somewhat higher risk for developing MS.

Visual evoked response: A delay in the P100 of the visual evoked response (VER) is the electro physiologic manifestation of slowed conduction in the optic nerve as a result of axonal demyelination (Klistorner et.al. 2008). This test was not usually helpful in the diagnosis of acute optic neuritis, unless there was a suspicion that the visual loss was functional.

Abnormalities in the VER could persist after recovery of full vision. At one year, 80 to 90 percent was abnormal, 35 percent returned to normal at two years (Brusa et.al.2001,Hickman et.al.2004 and Celesia et.al. 1990).The VER was often employed to find evidence of previous, asymptomatic, episodes of optic neuritis but the sensitivity and specificity were imperfect (Balcer,2006).

The multifocal VER was a technical advance that appears to be more sensitive and specific for identifying optic neuritis but this technology was not generally available. (Balcer, 2006 and Fraser et.al.2006).

Optical Coherence tomography :

Optical Coherence Tomography (OCT) measures the thickness in the retinal nerve fiber layer and detects thinning in most (85 percent) of patients with optic neuritis (Klistorner et.al.2008,Costello et.al.2006,Trip et.al.2005,Fisher et.al.2006 and de Seze et.al.2008). Lower values correlated with impaired visual outcome. However, its utility as a prognostic tool was limited in that abnormal values did not show up until early swelling disappears. In one study, OCT was less sensitive than VER in detecting subclinical optic neuritis (Naismith et.al.2009).

Aquaporin-4-specific serum autoantibody: Patients with recurrent optic neuritis may be particularly at risk for the variant of MS known as neuromycelitis optica or Devic's disease. This is particularly true for patients with a normal brain MRI and those with optic neuritis events in rapid succession (Pirko et.al.2004). In one study, seropositivity for the aquaporin-4-specific serum autoantibody was predictive of subsequent NMO among patients with recurrent optic neuritis (Matiello et.al.2008). This test has been suggested for individuals with recurrent ON, particularly if MRI is negative (Petzold et.al.2010).

The most common pathologic basis for optic neuritis is inflammatory demyelination of the optic nerve.

The pathology is similar to that of acute multiple sclerosis (MS) plaques in the brain with perivascular cuffing, edema in the myelinated nerve sheaths and myelin breakdown. Inflammation of the retinal vascular endothelium can precede demyelination and is something visibly manifests as retinal vein sheathing (Lightman et.al.1987). Myelin loss exceeds axonal loss.

It was believed that the demyelination in optic neuritis is immune –mediated, but the specific mechanism and target antigen(s) were unknown. Systemic T cell activation was identified at symptom onset and precedes changes in the cerebrospinal fluid (Roed et.al.2005).Systemic changes also normalize earlier (within two to four weeks) than central changes. T cell activation leads to the release of cytokines and other inflammatory agencies. B cell activation against myelin basic protein is not seen in peripheral blood but can be demonstrated in the cerebrospinal fluid of patients with optic neuritis (Soderstrom et.al.1993).

Diagnosis of Multiple Sclerosis in Children.(Grant Liu 2011

1. Clinical evidence

2. Positive MRI by the Mc Donald (2001) criteria 3 of 4 of

i. Nine or more white matter lesions or one gadolinium enhancing lesion

ii. three or more periventricular lesions

iii. one juxtacortical lesion or

iv. an infratentorial lesion.

3. Combination of abnormal CSF (oligoclonal bands or an elevated IgG index) and two lesions on MRI, of which one must be in the brain.

Dissemination in time can be demonstrated by either:

1. Clinical evidence

2. A new T2 or contrast-enhancing lesions which develops at least 3 months after the initial clinical event.

The events must not satisfy the diagnosis of ADEM which is a demyelinating or inflammatory event and includes white or gray matter lesions on MRI which is i) Polysymptomatic and ii) includes encephalopathy (i.e. behavioral or mental status change). Multiple events of this type would be more appropriately termed recurrent or multiphasic ADEM (Krupp et.al. 2007).

Neuromyelitis optica (NMO) must be excluded but it is unclear in children whether the absence of NMO-IgG antibodies excludes the diagnosis.

ACUTE Disseminated ENCEPHALOMYELITIS Vs.MULTIPLE SCLEROSIS

Post-infectious neurologic disease is not uncommon in children.
E.g. Acute cerebellar syndrome follows varicella infections, sensorineural hearing loss follows mumps infections and Sydenham's chorea was associated with streptococcal infections (Dale et.al.2000). Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease that typically follows an illness or vaccination. As opposed to MS, ADEM is typically a monophasic illness that does not require long –term treatment. ADEM was more common in children than adults (Dale et.al.2000).Although patients with ADEM could present with fulminate neurologic sign and symptoms, most patients had an excellent recovery.

The international Pediatric MS study group has defined ADEM by its clinical and radiographic features: encephalopathy, multifocal neurologic signs and large predominantly white matter, lesions on brain MRI, without

alternative explanations (Kelly,2006). When relapses after ADEM occur, such cases are difficult to distinguish from MS. The study group has defined ADEM as a single episode lasting up to 3 months. New symptoms may appear during this timeframe.

Children who have a second episode involving the same clinical and radiographic areas are diagnosed with recurrent ADEM. If different areas are affected, the child has multiple ADEM.

CONVERSION RATE TO MULTIPLE SCLEROSIS AFTER PEDIATRIC OPTIC NEURITIS

According to the ONTT, after acute unilateral optic neuritis, adults had a 50% chance of developing MS within 15 years (optic Neuritis Study Group 2008).

In contrast, the conversion rate to MS in children was unclear, perhaps due to the variability in study methodologies in published reports and because prospective data was lacking. One pediatric study reported a low conversion rate to MS (4%); however, the mean follow-up was 13 months (range 1-41 months) (Lana_Peixoto et.al.2001). Another study calculated the risk of developing MS after childhood optic neuritis using Kaplan-Meyer methods (Lucchinetti et.al.1997).

The risk of MS was estimated to be 13% at 10 years, 19% by 20 years, 22% by 30 years and 26% by 40 years. A different study reported a two –year risk of 36% (Wilejto et.al.2006).

A fourth study reported 16% of their patients with optic neuritis had MS; however, the purpose of that study was to define the presentation and visual prognosis in children and children with a prior history of demyelinating disease were not excluded (Brady,1999).

In our retrospective study (Bonhomme et.al. 2009), 18 patients were followed for more than 24 months and 3 of the 18 (17%) developed MS.

WHITE MATTER LESIONS ON MRI ARE PREDICTIVE OF RISK OF MS IN CHILDREN.

As established by the Optic Neuritis Treatment Trial (ONTT), an abnormal baseline brain MRI with white matter lesions is a strong predictor of MS after isolated optic neuritis in adults. 15 years after a bout of optic neuritis, 72% of adults with one or more brain MRI lesions at presentation developed MS, in contrast with a 25% conversion rate in those with no lesions (Optic neuritis Study Group 2008). In children, an abnormal MRI at presentation is likely also predictive.

Mikaeloff et.al. (2004) studied 296 patients after a first demyelinating event.

Patients were ultimately diagnosed with MS using Poser's criteria, ADEM (defined as polysymptomatic onset with mental status change and poorly limited lesions on MRI with thalamus or basal ganglia involvement), or a single focal episode. Similar to the optic neuritis data, there were age differences between the patients with MS (12 years, SD 3.4) and ADEM (7.1, SD 4.3). 22 % of the patients presented with optic neuritis.

Of the patients with optic neuritis at presentation, 86.6% were ultimately diagnosed with MS, whereas as 9% had monophasic ADEM. At the conclusion of the study, 53% of patients met diagnostic criteria for MS. The authors concluded that age of onset greater than 10 years, presence of an optic nerve lesion and the presence of well-defined periventricular and/or subcortical lesions on MRI were associated with conversion to MS.

Wilejto et.al. (2006) reported through their study that none of the patients with a normal brain MRI at presentation developed MS (although 1 developed NMO). All of the patients who presented with optic neuritis as the first manifestation of MS had at least 1 lesion on their initial MRI of the brain. Four patients with MRI lesions in the brain at presentation did not develop subsequent clinical attacks or further radiographic evidence of MS.

Of this subgroup, 2 patients initially met Mc. Donald's criteria for dissemination in space and the other 2 patients had multiple lesions (one with 6 lesions and one unavailable to the investigators for further review). None of these patients developed new ADEM were included in this study.

Bonhomme et.al. 2009 reviewed the medical records of children (<18 years) presenting with optic neuritis between 1993 and 2004 at the Children's Hospital of Philadelphia. Children with a history of demyelinating disease or prior optic neuritis were excluded. Symptoms, ophthalmologic findings, MRI findings and clinical outcomes were recorded.

They identified 29 consecutive children with idiopathic optic neuritis. Eleven patients (38%) had white matter T2/FLAIR lesions in the brain (not including the optic nerves). 18 patients were followed for more than 24 months and as stated above, 3 of the 18 (17%) developed MS. All three patients had an abnormal brain MRI scan at their initial presentation of optic neuritis. None of the patients with a normal brain MRI scan at presentation developed MS over an average follow-up of 88.5 months. Patients with one or more white matter lesions on MRI were more likely to develop MS (3/7 vs.0/11,p=0.04,Fisher's exact test). It was concluded that children with brain MRI abnormalities at the time of the diagnosis of optic neuritis had an increased risk of MS.

BILATERAL VS. UNILATERAL OPTIC NEURITIS, OR AGE AS RISK FACTORS.

Compared to adults, bilateral ON is more common in children and is often simultaneous. It has been suggested that unilateral ON carries a greater risk for the development of multiple sclerosis (MS) in children compared to bilateral ON, but age may be a confounder.

Waldman et.al.2009 performed a meta-analysis to determine whether age is a risk factor for unilateral vs. bilateral simultaneous optic neuritis and establish the risk of multiple sclerosis in children after unilateral vs. bilateral optic neuritis.

Logistic regression was used to determine the risk of MS after unilateral vs. bilateral ON, adjusting for age and MRI abnormalities with 227 patients. After unilateral ON as a first demyelinating event compared to bilateral ON, children were perhaps more likely to develop MS (OR 2.0,p=0.07).However, unilateral ON occurred more frequently in older children (OR 1.26,p<0.0001).

After adjusting for age, the risk of MS after unilateral vs. bilateral ON was not significant (OR=1.67,p=0.2).For every 1 year increase in age, the risk of MS significantly increases in children with abnormal brain MRI scans at

presentation (OR 30.0,p=<0.0001).Thus, the relation between unilateral vs. bilateral ON and the development of MS is dependent upon age. Unilateral ON is more common in older children; this population may be at greater risk for MS, especially in those children with brain MRI abnormalities at presentation.

Bonhomme et.al.2009 reported through their study of pediatric optic neuritis that nine patients (31%) had relapses of optic neuritis during the study period and 5 had more than one relapse. The pattern and location of the recurrent episode showed no specific pattern. For example, 3 patients who initially presented with bilateral optic neuritis had subsequent unilateral relapses.

In contrast, the remaining 6 patients presented with unilateral optic neuritis, half of whom ultimately met criteria for bilateral sequential optic neuritis and the other half for recurrent optic neuritis. Of the nine patients with recurrent optic neuritis, two patients developed MS.

The relative risk of developing MS among patients with optic neuritis recurrence was 4.0(p=0.25). It was unclear whether this would be confirmed in larger cohorts. Patients with bilateral simultaneous or sequential optic neuritis did not have a greater risk of MS compared to patients presenting with unilateral disease (p=0.53).

A POSSIBLE PEDIATRIC OPTIC NEURITIS TREATMENT TRIAL

In order to resolve the controversy concerning the benefit of corticosteroids for pediatric optic neuritis and to establish appropriate treatment guidelines, a multi centre Pediatric Optic Neuritis Treatment Trial (PONTT) is needed.

In such a trial, patients can be randomly assigned to one of three treatment groups, consisting of two corticosteroid groups and a placebo group:

1. IV methylprednisolone group:1000 mg/day or 30 mg/kg/day (depending upon the child's weight) for 3 days followed by a 15 day prednisone taper (starting at mg/kg).
2. Oral methylprednisolone group:1136 mg/day or 34 mg/kg/day (depending upon the child's weight) for 3 days followed by 15 day prednisone taper (starting at 1 mg/kg).
3. Oral placebo: inert substance given using the same schedule as the oral placebo group.

Primary end points will be related to visual function and OCT measurements but secondary outcome measures will be related to conversion to multiple sclerosis.

Prognosis

The long term visual prognosis of idiopathic optic neuritis remains good. More than 90% of the patients recover a visual acuity of 20/40 or better by 6 months, as seen in the ONTT. A cut off level of vision <_ -20/50(6/15),contrast sensitivity of<1.0 log units and a visual field mean deviation of <_ -15 dB after one month in the ONTT were predictive of a poor visual outcome at 6 months, a prediction that could not be made with any certainty at baseline.

PART - II

AIM

Evaluate the clinical profile and assess the visual outcome of Optic Neuritis in Children.

OBJECTIVES

1. To study the clinical presentation of paediatric optic neuritis
2. To assess the visual acuity
3. To identify associated systemic features
4. To study the MRI findings
5. CSF analysis
6. To assess the visual outcome after intervention

METHODOLOGY

This chapter explains the materials and methods and procedures adopted for the research study. Based on the objectives framed for the study, the methodology was designed to arrive at the possible results so as to explain the stated objectives clearly.

This chapter comprises the content with the following sub captions viz., selection of locale of the study, selection of respondents for the study, inclusion process of respondent, exclusion process of respondent, variables selection and their possible measurement procedures and the statistical tests used for analyzing the data for furnishing the results in meaningful way as well as to satisfy the objectives of the study.

Selection of locale: The Regional Institute of Ophthalmology and Government Hospital, Egmore was selected as the locale of the study as this is only out- patient Govt. hospital in and around Chennai.

Selection of Respondents: Peadiatric out patients with symptoms and signs of optic neuritis under the age group of 18 years of both the sexes were selected as respondents. Altogether 15 respondents during the study period of one year were considered for collecting data for the study.

Sample size and sampling procedure: A sample size of 15 out patients with accidental sampling procedure was adopted to select the respondents.

Accidental sampling procedure: This is a non - probabilistic sampling procedure which prescribes the procedure of selecting the respondents by fixing some criteria for the selection of respondents. Accordingly, the following criteria were fixed to satisfy the selection of a respondent.

i. the respondent should be under the age group of below 18 years
ii. the respondents should be both sexes
iii. the respondent should have optic neuritis signs and symptoms.

The above criteria were considered for selecting the respondents. Accordingly, the out- patients satisfying aforesaid criteria were selected till attaining a sample of 15 numbers for the study.

INCLUSION CRITERIA:

The out patients with the following criteria were included in the study

Paediatric patients (<18 years) with clinical features of optic neuritis –

- Central visual loss
- Loss of colour vision
- Central Scotoma
- Swollen or pale optic disc
- Afferent pupillary defect.

EXCLUSION CRITERIA:

The following signs and symptoms of patients were excluded from the study

1. Patients with hereditary optic neuropathy
2. Patients with systemic vasculitis
3. Patients with optic nerve sheath tumours, neuroblastoma, leukaemia and Histiocytosis
4. Patients with sinusitis, orbital cellulitis, and juvenile rheumatoid arthritis
5. Malnutrition
6. Retinal exudates or other retinal lesions

SCREENING PROCEDURES / VISITS: The following procedures and methodology were adopted to investigate the cases and collect data for the study.

- Detailed history of present and past illness

- Visual acuity using Snellen's acuity chart / paediatric picture chart

- Pupillary reaction for presence of Relative Afferent Pupillary Defect

- Colour vision using Ishihara's pseudo isochromatic plates

- Visual fields using Automated Perimetry by Octopus

- Intraocular pressure using Goldmann Applanation tonometer

- Slit lamp examination of anterior segment, lens and vitreous

- Direct and Indirect ophthalmoscopy :

Size, shape, margins of the disc, hyperemia, edema of the disc was assessed. Associated retinal edema, hemorrhages and exudates or any other associated pathology were looked for in ophthalmoscopy.

• Colour fundus photography :

Serial fundus photographs at the time of presentation, at 2 weeks and 6 months follow up were taken. Thus disc changes were objectively recorded.

• MRI of the brain:

An abnormal brain magnetic resonance imaging (MRI) older age, oligoclonal bands in cerebrospinal fluid and elevated immunoglobulin G index were associated with multiple sclerosis outcome.

Children with monosymptomatic optic neuritis and an abnormal brain MRI had a higher risk for multiple sclerosis. These children were monitored closely for the subsequent diagnosis of multiple sclerosis and can be considered for early preventive therapy.

• CSF analysis :

All children were subjected to CSF analysis to look for elevated cells, proteins and oligoclonal bands thereby aiding in diagnosing etiology of optic neuritis.

At the initial visit, a detailed systemic evaluation was performed to assess systemic risk factors. Where indicated, other systemic or neurologic investigations will be done to rule out any systemic or neurologic cause of visual loss.

All the fifteen children were treated with Iv methyl prednisolone 4mg/kg per day for 3 days followed by a dose of oral prednisolone 1mg/kg for 11 days tapered over a two week period. Some controversy persists concerning the exposure of children to high-dose parenteral corticosteroids to treat an entity that is usually self-limited, but given the severity of vision loss in one or both eyes in this population, this intervention is standard in neuro-ophthalmological practice

FOLLOW UP:

The patients were examined in every two weeks for the first month and subsequently every monthly visit for six months.

ASSESSMENT OF PARAMETERS**:**

1. Improvement in visual acuity

2. Improvement in colour vision

3. Improvement in visual fields

4. Fundus photography to assess optic disc edema

5. Assessment of pupil

Variables selected and their measurement:

Age : age of the patient was taken as the chronological years he/she completed at the time of investigation from his/her birth. This was noted in the completed years as such.

Sex: sex of the patient was noted as male or female in the form of nominal distribution procedure.

Associated febrile illness preceding optic neuritis within a 2 week period or neurological features such as weakness of limbs, tingling or numbness in extremities was noted.

Unilateral or bilateral involvement of the disease was noted for all patients

Pain on Extra ocular movement during the disease process

Number of recurrences since the time of presentation to the end of follow up period were also recorded.

Colour vision and fields could not be recorded for most of the patients because their presenting visual acuity was very poor

Ethical committee: the entire research project outline was submitted before the ethical committee of the institution and got approved. The instructions to the researcher, respondents and other modalities are presented in the appendix.

Statistical analysis: simple frequency analysis for explaining the number cases and percentage analysis of data was done. Non parametric tests like rank order correlation, x2 tests were done to interpret the data..

RESULTS

This chapter deals with the results obtained in the study. The results are pertaining to the objectives stated for the study. By administering appropriate statistical tests and hypothesis developed, the results are carefully analysed and presented in the following pattern:

The distribution of respondents' personal profile such as age, sex, laterality, pain on eye movement, associated features of disease, CSF analysis, MRI observation results, Causes of optic neuritis, Association between recurrences and disease incidences, Association between visual acuity and disease occurrence, association between recurrence of diseases with associated factors, details of visual outcome due to treatment and optic disc appearance at six months.

Table.2.Distribuion of Age of the respondents

Age category	No.(n=15)	Per cent
3 – 5 yrs	5	33.34
5 – 10	5	33.33
10 – 15	5	33.33

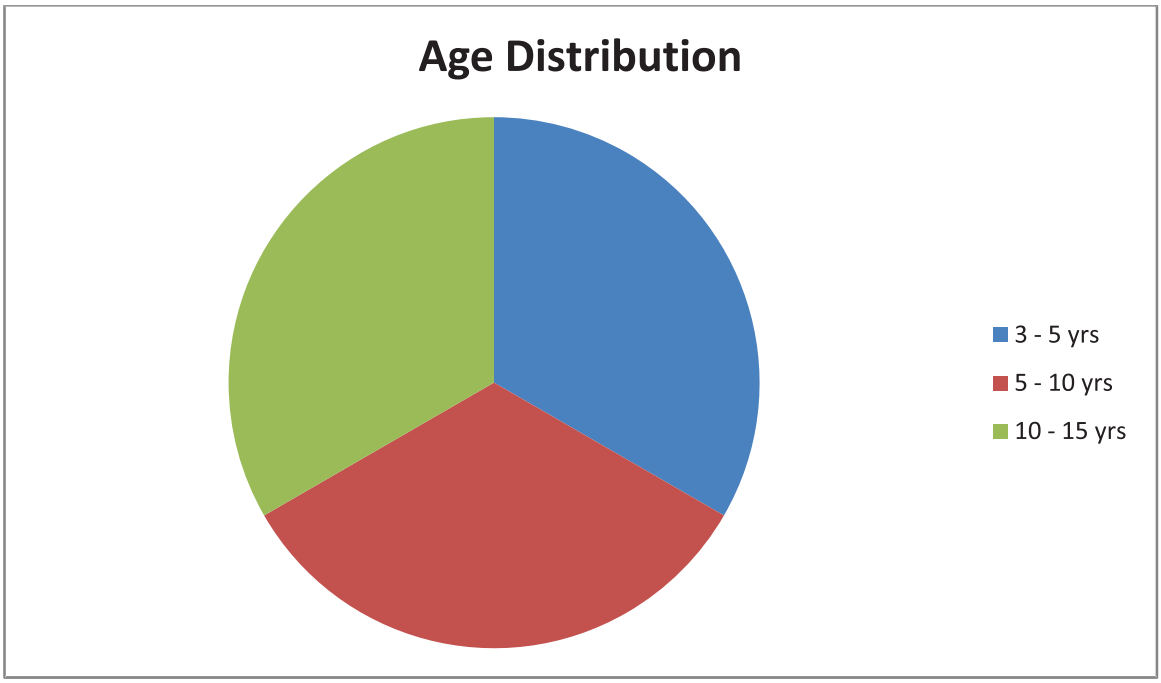


Fig.2 Distribution of Age in respondents

Analysing the age distribution of the respondents selected for the study equal percentage of respondents (33.33%) fell under the age categories of 3 to 5, 5 to 10 and 10-15 years.

Table.3. Gender distribution of respondents

Description	No.(n=15)	Per cent
Male	5	33.33
Female	10	66.67

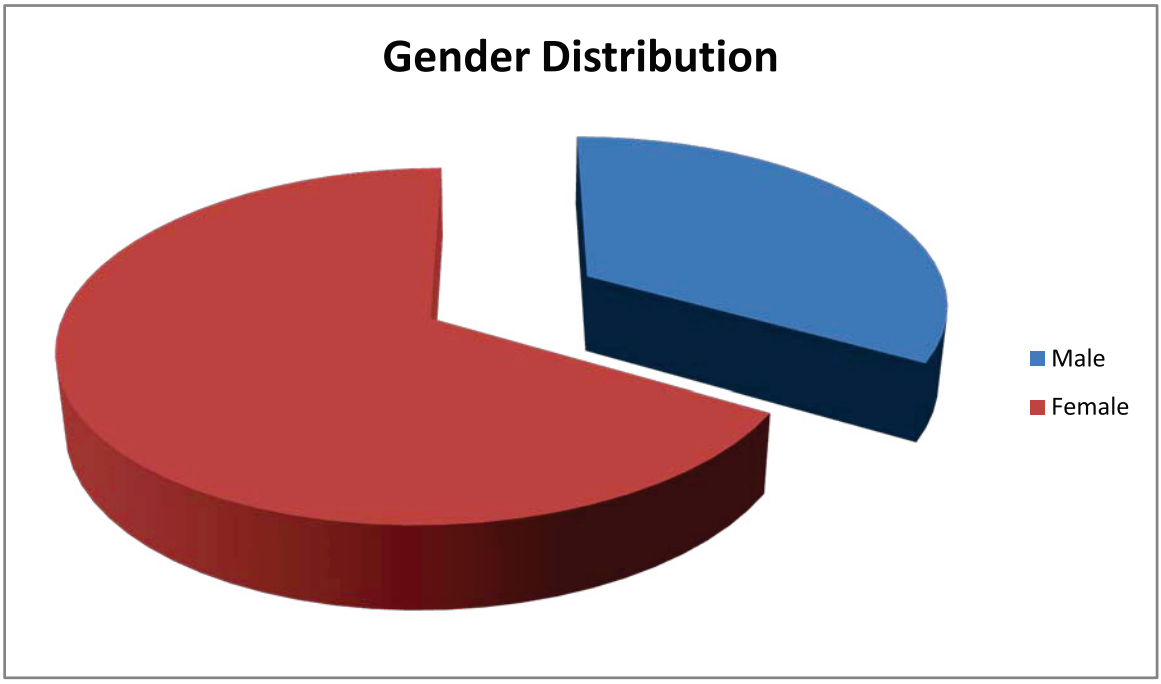


Fig.3. Gender distribution in respondents

Of the sampled respondents for the study, the distribution of female accounts for 66.67per cent and the remaining of them belong to male category.

Table.4. Distribution of laterality of respondents

U/L or B/L involvement : n=15

Description	No.(n=15)	Per cent
Unilateral	6	40.0
Bilateral (no. of eyes)	9 (18)	60.0

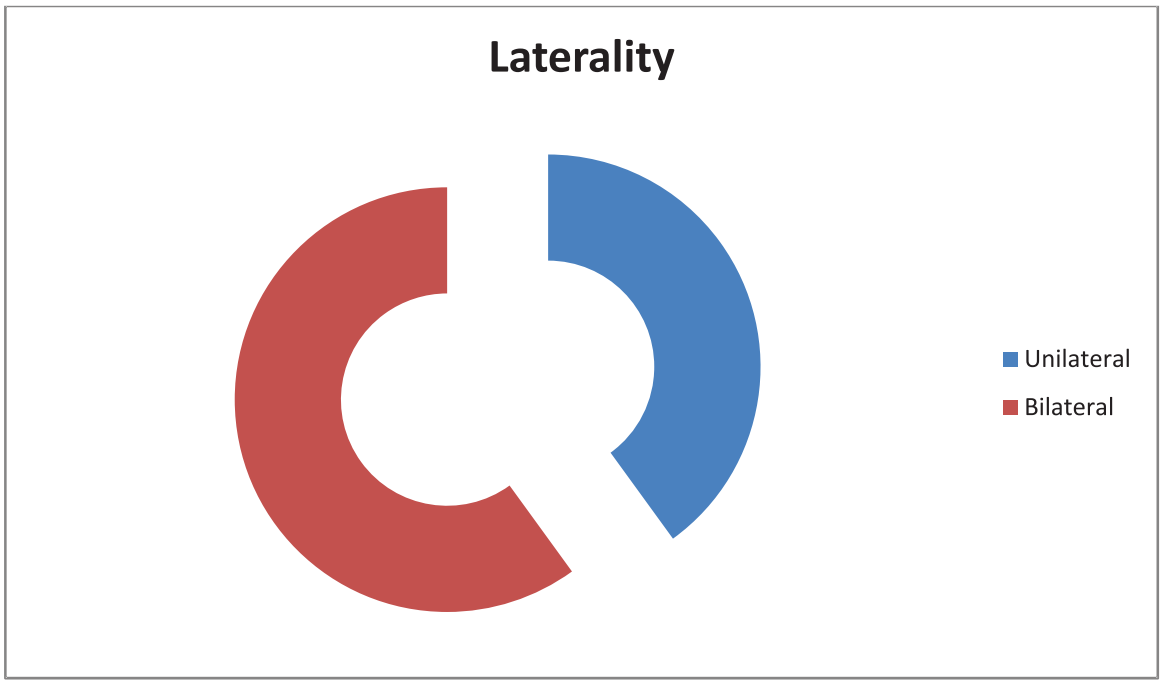


Fig.4 Laterality of Optic neuritis

Analysing the table on unilateral and bilateral involvement in optic neuritis, it was observed that 60 per cent of the respondents had bilateral involvement and the remaining 40 per cent of them had only 40 per cent unilateral involvement.

Hence it is inferred that most of paediatric optic neuritis was bilateral in most of the cases.

Compared to adults, bilateral ON is more common in children and is often simultaneous. It has been suggested that unilateral ON carries a greater risk for the development of MS in children compared to bilateral ON, but age may be a confounder.

Table 5 :Visual Acuity At Presentation :

Visual Acuity	Percentage (n=24)
No PL	25% (6)
PL +	20.83 % (5)
Hand Movements	20.83% (5)
CFCF – 1/60	29.16% (7)
>= 2/60	4.16% (1)

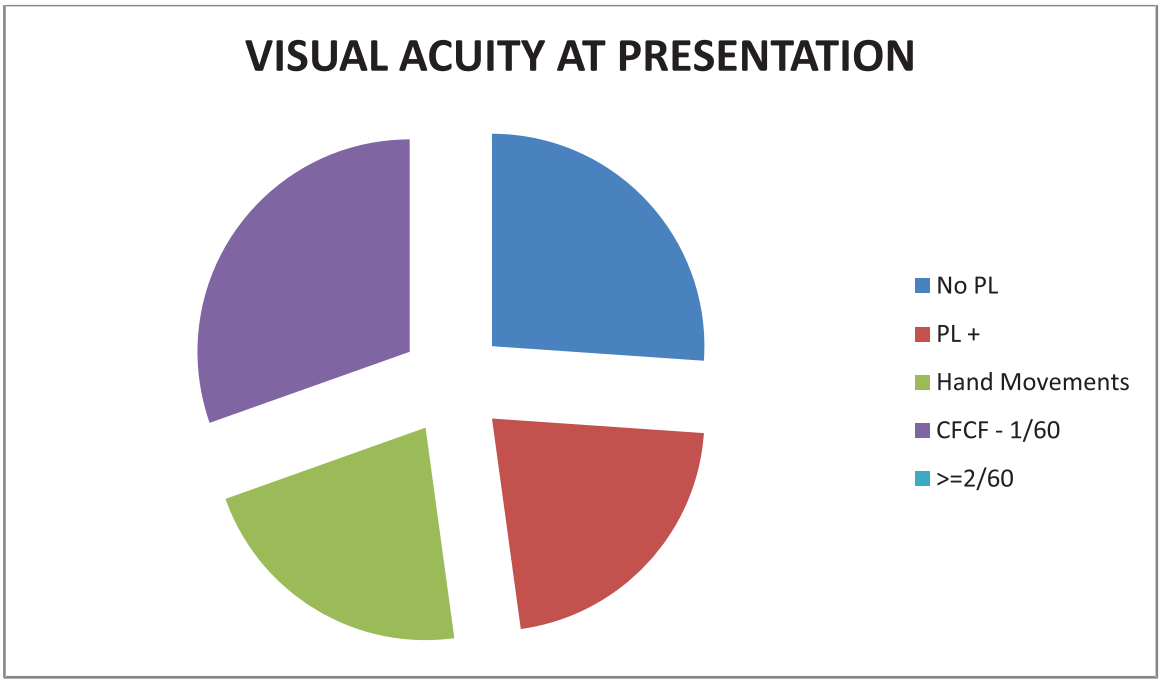


Fig.5 Visual acuity at Presentation

The presenting visual acuity in children with optic neuritis was very poor. The presenting visual acuity ranged from no perception of light to 1/60.

Colour vision and fields could not be recorded in children with optic neuritis due to very poor vision at presentation.

Table.6. Distribution of respondents expressing pain on eye movement

Description	No. (n=15)	Per cent
Present	4	26.67
Absent	11	73.33

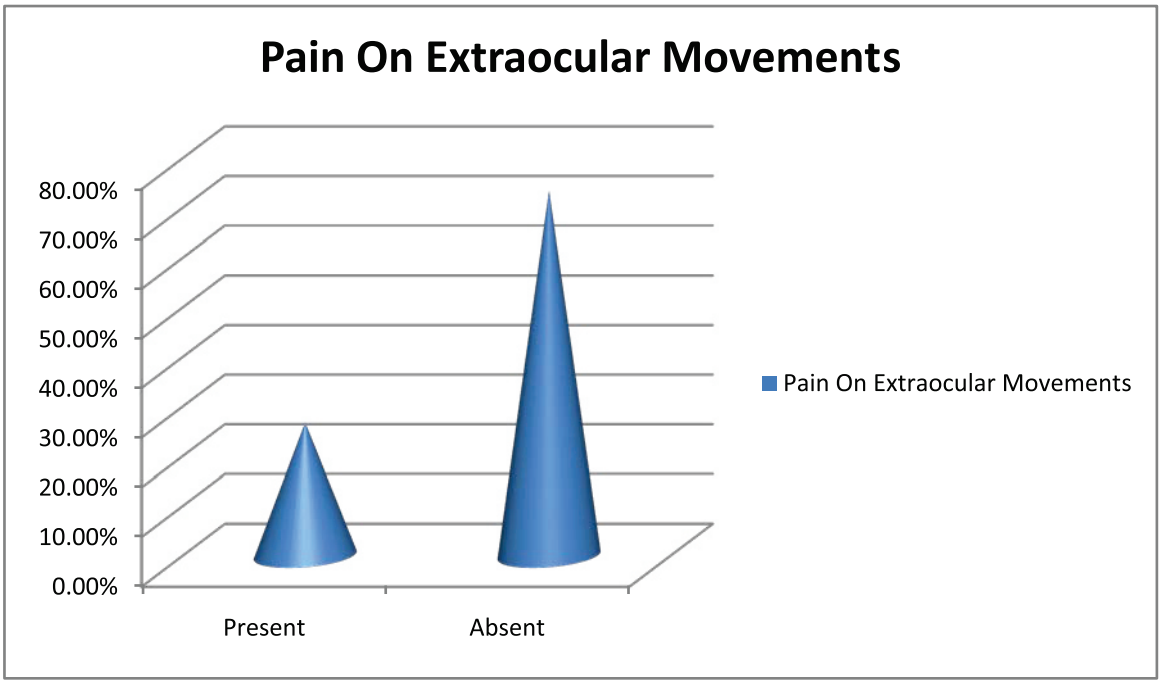


Fig.6 Pain on extra ocular movement

The observation on the feeling of pain of the respondents of optic neuritis vide table.4 explicitly exhibited that maximum number of them (73.33%) had no pain and the remaining 26.67 per cent of them had expressed the presence of pain in the eyes. Hence it is inferred that most of the cases in paediatric ON did not express pain on extra ocular movements.

Table.7. Associated features of optic neuritis patients

Description	No.(n=15)	Per cent
Febrile illness	3	20.0
Neurological Symptoms	4	26.67
Nil	8	53.33

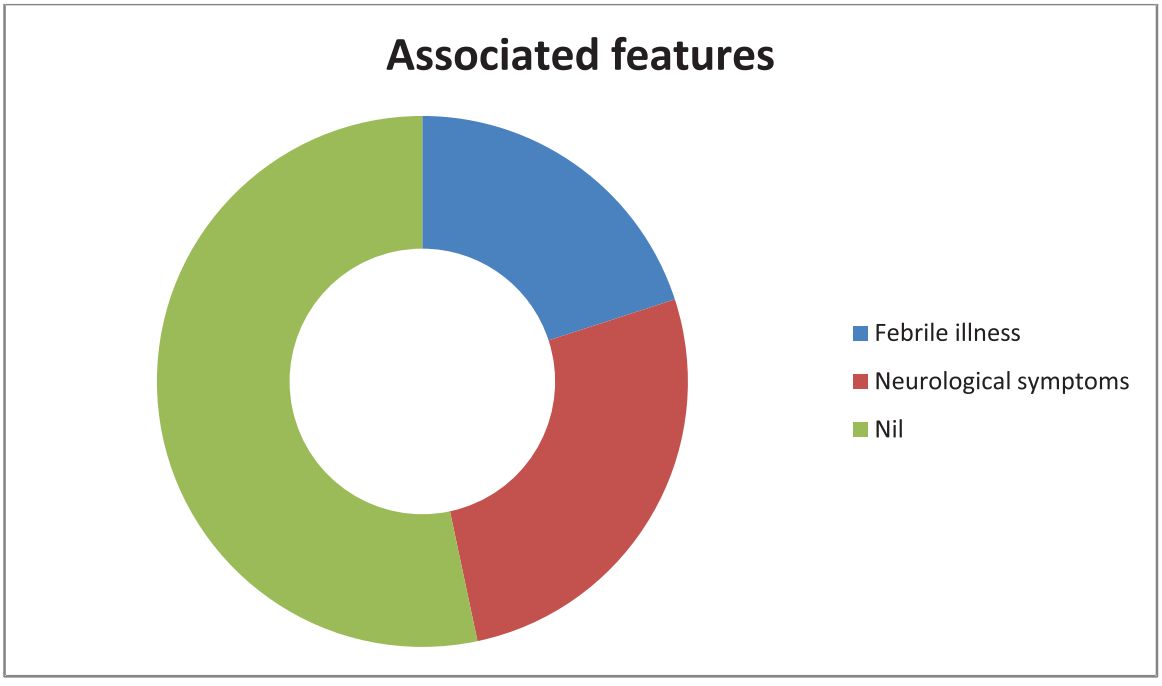


Fig.7. Associated features of disease.

The assessment of associated features of optic neuritis suffering respondents revealed that more than half of the sampled cases had no associated features. More than one fourth of them (26.67 %) had neurological symptoms and one fifth of them (20%) had febrile illness as associated features. Hence it is inferred that febrile illness and neurological symptoms were preceding factors associated with paediatric ON.

Table.8. Description of CSF analysis

Description	No. (n=14)	Per cent
Normal	10	71.43
Raised Protein	3	21.43
Oligoclonal band	1	7.14

The CSF analysis revealed that out of total sampled patients, most of them (71.43%) were having no symptom. Whereas only one fifth of them had (21.43%) raised protein and only seven percent had Oligoclonal band. Hence it is inferred that the CSF analysis proved the etiology of ADEM and MS as a cause of optic neuritis in children.

Table.9. Types of lesions observed through MRI

Lesion	No. (n=14)	Per cent
Hyperintese lesions of brain & spinal cord	5	35.71
Hyperintense lesions of spinal cord alone	3	21.43
Normal	6	42.86

The MRI scan report depicts through the table that 42.86 per cent of the sampled patients had normal vision without any symptomotological evidences. More than one third of the sampled patients had Hyper intense lesions of brain and spinal cord. Whereas 21.43% of the cases were having Hyper intense lesions of spinal cord alone. It is inferred that MRI precisely projects the causes of optic neuritis through more than half of the sampled respondents' brain and spinal cord lesions.

Table.10. Causes of Optic neuritis

CAUSE	NO.(n=14)	Per cent
ADEM	5	35.71
Devics	2	14.29
Isolated ON	5	35.71
Multiple Sclerosis	2	14.29

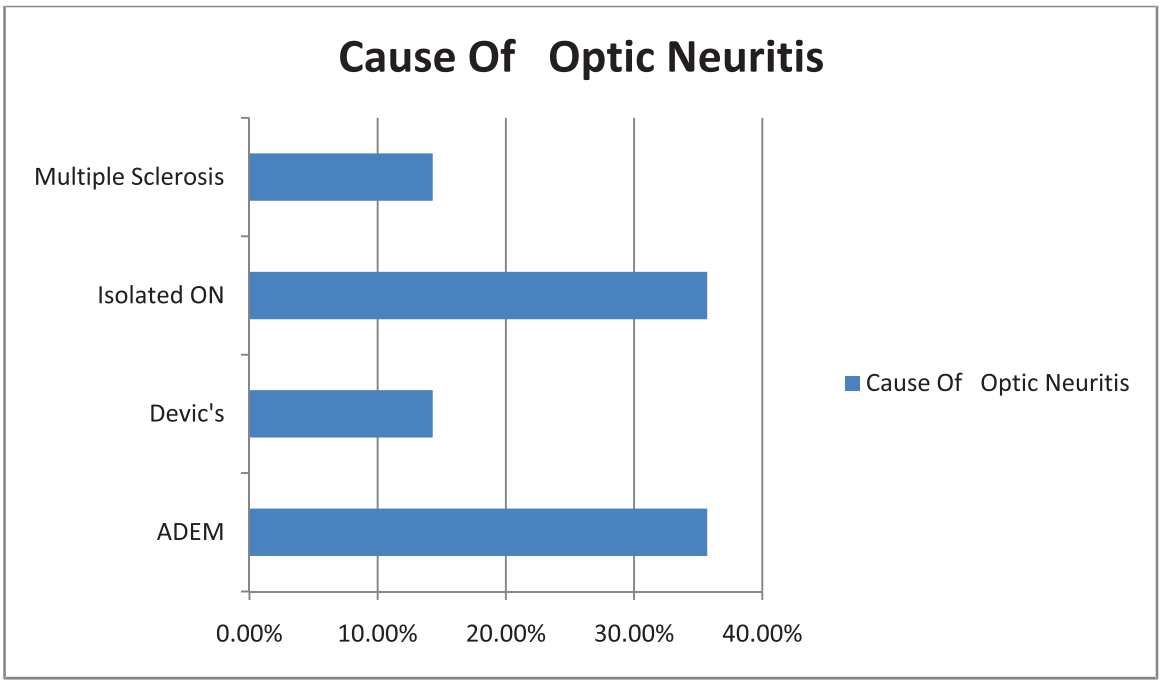


Fig.8. Causes of Optic Neuritis

The table explaining the causes of optic neuritis significantly revealed that both ADEM and Isolated ON individually caused each 35.71 percent and altogether

About two third of the respondents had the causes of optic neuritis by ADEM and Isolated ON, whereas the Devic's diseases and MS were the causes for optic neuritis each 14 percent of cases.

Hence it is inferred that the causes namely ADEM and Isolated ON were the major etiology of paediatric optic neuritis.

Table.11. Association between recurrence of causes and the disease incidences

N.A.	ADEM	Devic's disease.	Isolated ON	M.S.	ON	Total
Recurrence						
0	1	4	0	4	0	1	10
1	0	0	1	0	2	0	3
2	0	1	0	0	0	0	1
3	0	0	1	0	0	0	1
Total	1	5	2	4	2	1	15

X2=21.8* Significant @10% level

The association between the diagnostic causes revealed through the table that there exists a significant association between recurrences of the causes and the disease incidence at 10 per cent level of significance in chi-square test. This indicates that even though, there is no recurrence,40% of the patients had suffered from ADEM and 40% had suffered from Isolated ON and only 10% will not be having symptoms not detectable (NA) and 10 per centhad O.N.

If there is one time occurrence,33% had ADEM and 66% had M S Further recurrence will also be indicative of ADEM. When a maximum recurrence of 3 was detected, the major cause for visual acuity turned out to be Devic's disease. Hence it is inferred that causes and disease recurrence had significant relationship. The number of occurrences also revealed the etiology of pediatric ON respectively for ADEM, MS, Devics disease with once twice and thrice occurrences.

Table.12.Association between visual acuity and disease occurrence.

	N.A.	ADEM		Devic disease.	Isolated ON	M.S.	ON Total
Visual Acuity							
0.03	0	0	0	0	1	0	1
0.05	0	1	0	0	0	0	1
0.15	0	0	0	0	1	0	1
0.2	0	0	1	0	0	0	1
0.3	1	1	1	0	0	0	3
0.4	0	1	0	0	0	0	1
0.9	0	1	0	2	0	0	3
1.0	0	1	0	2	0	1	4
Total	1	5	2	4	2	1	15

X2=32.25 N.S.

Visual acuity was enhanced following treatment with steroids. Hence visual acuity and disease are independent and not influencing. Hence it is inferred that visual acuity was free from disease occurrence.

Table.13.Association between Recurrence of diseases and associated factors

Recurrence	Associated factors			
	0	1.0	2.0	Total
.00	7	3	0	10
1.0	1	0	1	2
3.0	0	0	3	3
Total	8	3	4	15

X2 value=12.75 N.S.

The chi-square value is not significant and hence the associated factors are not influencing the recurrences of the diseases. Both are independent in nature.

Table.14.Details of treatment effects with different period on visual outcome.

VISUAL OUTCOME WITH TREATMENT

Presenting vn	Post treatment 1 week	1 month	6months	Remarks (Pattern of recovery)
RE 1.5/60 LE HM +	BE 6/6	BE 6/6	BE 6/6	A1
RE No PL	6/9	N.A.	6/24	B1
BE 1.5/60	RE 6/36 LE 6/9	6/18	6/18	A3
RE PL +	6/60	6/60	2/60	B5
RE 1.5/60 LE 6/36	BE 6/6	6/6	6/6	A2
BE No PL	RE6/60 LE HM+	RE 6/36 LE 6/60	RE 6/36 LE 5/60	B2
BE HM+	BE 6/6	6/6	6/6	A1
RE 1.5/60 LE HM+	BE 6/9	6/9	6/9	A4
LE CFCF	6/12	6/9	6/9	C1
BE No PL	RE PL+ LE HM +	RE PL+ LE 6/60	RE PL+ LE 4/60	B3
LE No PL	6/18	6/18	6/18	B4
RE HM +	6/9	6/9	6/9	A4
BE PL +	RE 6/12 LE 6/9	RE 6/12 LE 6/9	RE 6/12 Le 6/9	B6

The table depicts the visual recovery pattern of children after the treatment with the observation taken in the post treatment intervals of one week, one month and six months duration.

The remarks column in the table indicates the different presenting vision patterns like
Hand movement and with slight vision ability(1.5/60) denoting symbol ‘A’,
Presence or absence of light denoting symbol ‘B’ and
Counting fingers close to face denoting symbol ‘C’.

The subscript numbers with each symbol indicates the pattern of recovery of vision after the treatment denoting similar letter for similar recovery pattern and different numbers for different recovery patterns.
Accordingly, the visual recovery observation of children in different intervals after the treatments is explained as follows:

Pattern A1: The children with vision ability at the time of presentation were having the vision score of 1.5/60 (RE)+hand movement(LE) perception and perception of Hand movement alone in both eyes had the visual recovery pattern of 6/6 in all the intervals of one week, one month and six months intervals in both the cases.

Pattern A2 : The visual ability at the presentation of the case was with snellen score of RE 1.5/60 and LE 6/36. The recovery pattern after the treatment during different intervals was with the score of 6/6 in both the eyes during all the observation intervals.

Pattern A3 : The children with visual ability of BE 1.5/60, had the recovery pattern after the treatment was 6/36,6/18 and 6/18 during one week, one month and six months intervals respectively in RE and the visual ability of 6/9 was observed in left eye at one week interval alone.

Pattern A4 : The visual ability of two cases were having the score of RE 1.5/60,and LE HM+, and the second case was with RE HM + alone. The treatment effect contributed the visual recovery of 6/9 in both the cases in all the intervals of time.

Pattern B1: This pattern represents the visual ability of no perception of light in the RE. Such case responded to treatment viz.6/9 in one week interval and 6/24 during six months interval.

Pattern B2: Here no perception of light in both the eyes. The treatment effect was different in pattern for the right and left eye respectively such as 6/60,6/36 & 6/36 and perception on hand movement,6/60 &5/60 on one week interval,one month and six months intervals.

Pattern B3 : This pattern has no perception of light on both eyes. The treatment response pattern was also different for RE and LE with visual recovery of perception of light in all the intervals in RE and hand movement perception,6/60 &4/60 in LE for one week, one month and six months intervals.

Pattern B4: This pattern exhibits no perception of light in LE. The treatment effect pattern was 6/18 in all the intervals consistently.

Pattern B5: Exhibits the visual acuity at the time of presentation with perception of light in RE. The visual recovery pattern after the treatment was 6/60 at one week and one month interval and 2/60 at six months interval.

Pattern B6 : The visual ability was perception of light in both eyes and the pattern of recovery was 6/12 in RE and 6/9 in LE for all the intervals of observations.

Pattern C1 :This pattern had CFCF in LE which responded to the treatment with visual recovery of 6/12,6/9 & 6/9 respectively for one week, one month and six months intervals.

Hence it is inferred that the recovery pattern of visual gain was positive and significantly responsive to the treatment irrespective of the visual ability before treatment.

Table.15. Optic Disc appearance at 6 months

Optic Disc	No. of eyes (n=23)	Percentage
Temporal Pallor	12	52.18
Optic Atrophy	4	17.39
Normal	7	30.43

The table depicts that out of total number of eyes (21) tested, more than half of the sample eyes tested were having the optic disc appearance with temporal pallor (i.e. more than 50% of the nerves were thin and weakened with 50% visual acuity) followed by 17.39% of the eyes had optic atrophy with total visual loss. Less than one third of the sampled number of eyes had normal vision without any appearance in the optic disc.

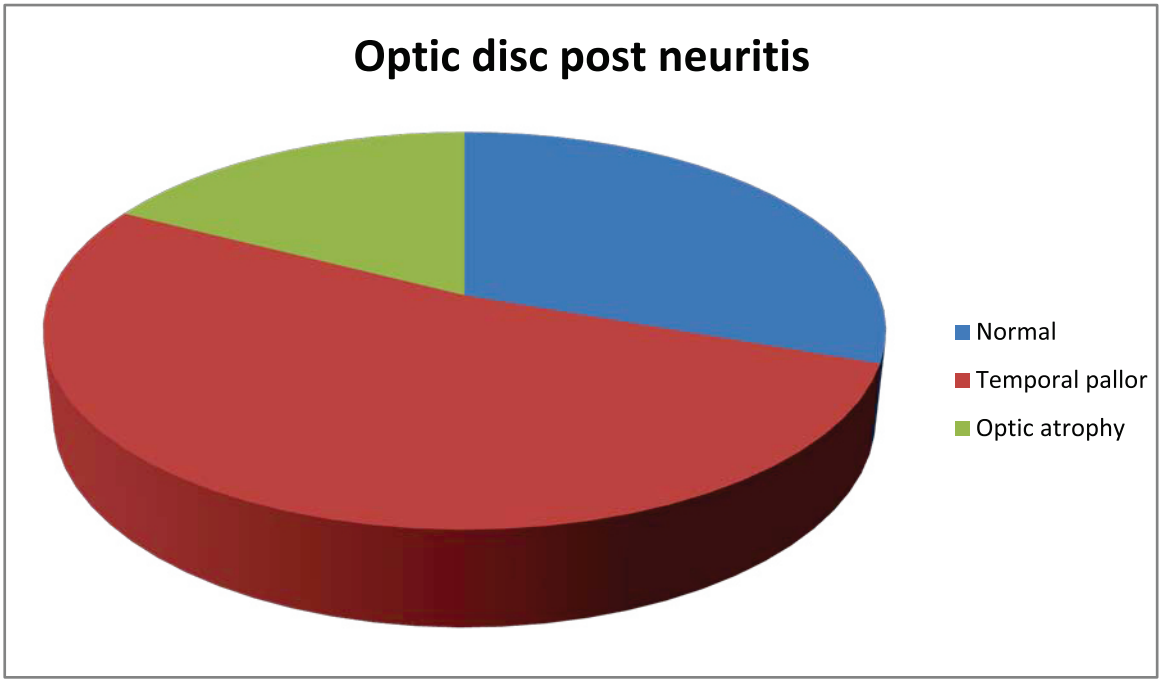
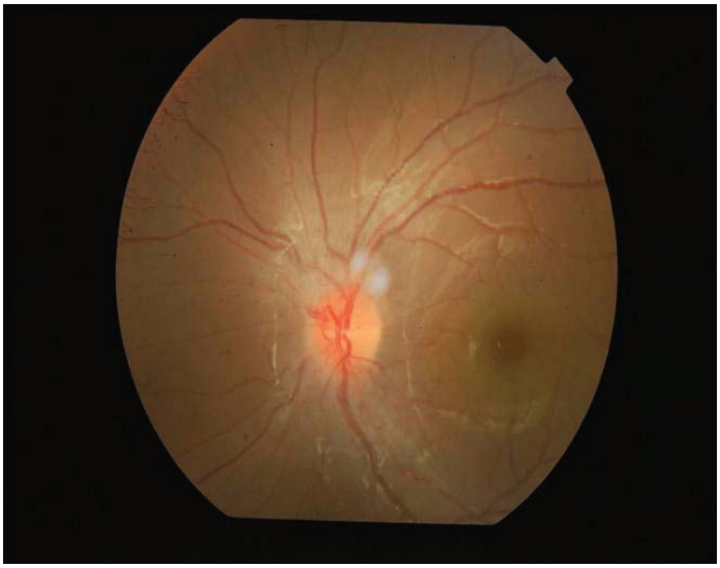


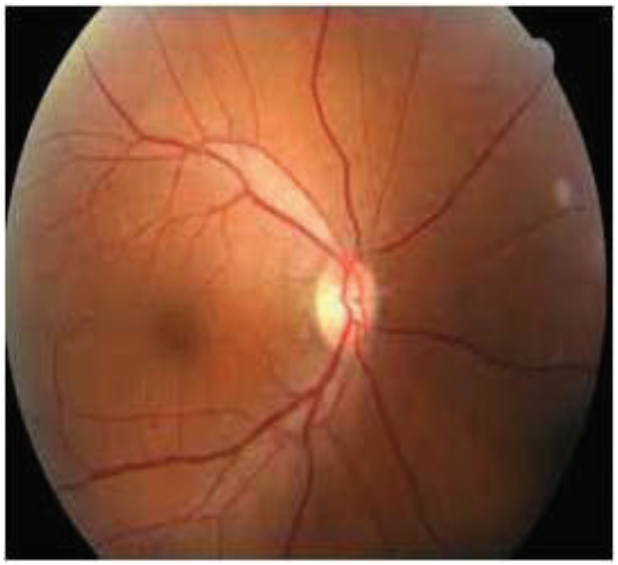
Fig. 9.Optic disc post neuritis at six months

Hence it is inferred that more than half of the sampled number of eyes had temporal pallor due to optic neuritis in children and nearly one third of them had normal vision.

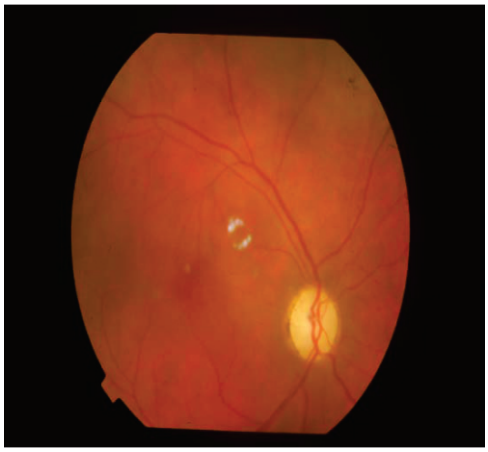
FUNDUS PICTURE SHOWING HYPEREMIC DISC WITH BLURRED MARGINS IN A CASE OF OPTIC NEURITIS (Case 1)



FUNDUS PICTURE SHOWING TEMPORAL PALLOR IN POST OPTIC NEURITIS (Case 6)



FUNDUS PICTURE SHOWING OPTIC ATROPHY IN A CASE OF RECURRENT OPTIC NEURITIS DUE TO MS (Case 10)



MRI SHOWING HYPERINTENSE LESIONS IN BRAIN AND SPINAL CORD (Case 3)

DISCUSSION

This chapter deals with the discussions related to the results obtained in the study. The discussions are carefully reasoned and substantiated with findings reported in earlier studies wherever necessary. The discussions are presented in the following pattern as in the case of results:

The distribution of respondents' personal profile such as age, sex, laterality, pain on eye movement, associated features of disease, CSF analysis, MRI observation results, Causes of optic neuritis, Association between recurrences and disease incidences, Association between visual acuity and disease occurrence, association between recurrence of diseases with associated factors, details of visual outcome due to treatment and optic disc appearance at six months.

Age distribution of respondents:

The results showed that the age group of respondents distributed equally and uniformly in all the categories of age group. This may be due to the reason that the study methodology prescribed the criteria that the age group of the respondent below the age group of 18 years old and the categorization of respondents was also rages from childhood to adulthood. These criteria might be influencing to have such results.

Gender distribution of respondents:

The results revealed that number of female children was more compare to their male counterpart in the sample selection. This may be due to the reason that female children were having more prone to optic neuritis problem than male children. This was supported by the study conducted in adults that female patients were more prone to optic neuritis than male adults. The same corollary this results would also explained.

The distribution of laterality:

The results of laterality confirmed that more children had bilateral involvement. This may be due to the reason that the optic neuritis affects both the eyes of children compare to adults. It is natural and many studies proved that paediatric optic neuritis had bilateral involvement. This study has more number of evidence and the results were in consonance with the earlier studies. This result was supported by de la Cruz and Kupersmith 2006 and Wilejto et.al.2001 that Bilateral optic neuritis was more common in children younger than 12 to 15 years old and also in Asian and black South African patients.

Pain on eye movement:

The result depicts that most of the sampled respondents had no pain but only one fourth of the respondents had pain. This may due to the reason that

respondents who expressed pain belonged to the age group of more than ten years. This result approaches the fact that the adult ON had pain on eye movements as evidenced by ONTT eye pain occurred in 92% of patients in the ONTT and often worsened with eye movement. The onset of pain generally coincided with the visual acuity loss and improved along with it.

Associated features of disease:

The result inferred the finding that the febrile illness and neurological symptoms were preceding factors associated with paediatric ON. The results of associated features with paediatric ON could be substantiated with the results of CSF and MRI analysis of this study that febrile illness was evidenced by ADEM and neurological symptom proved by MS/Devics disease.Further Dale et.al. 2000 reported that acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease that typically follows an illness or vaccination. As opposed to MS, ADEM is typically a monophasic illness that does not require long –term treatment. ADEM was more common in children than adults.

CSF analysis

The CSF analysis was mainly done in diagnosing the causes of optic neuritis like ADEM and MS. In this study the CSF analysis invariably proved the causes of ADEM and MS in 28% of cases out of sampled respondents. This

may be explained that the major causes of paediatric optic neuritis were ADEM and isolated ON. The similar type of result was observed by the Pediatric Multiple Sclerosis Study Group that in all probability it represents an example of mild acute disseminated encephalomylelitis and twelve of 20 patients with monophasic illness had isolated optic neuritis.

MRI observation results:

The results of MRI precisely project the causes of optic neuritis through more than half of the sampled respondents' brain and spinal cord lesions. The reasons for this result could be substantiated in the following past evidences conducted through proven research reports. The results of MRI in diagnosing paediatric ON could be explained in the same corollary of CSF analysis. Here the MRI could give more precision and Explain etiology of more number of cases as compared to CSF analysis. MRI analyses stand more reliable and valid. The long term prognosis of inflammatory demyelinating optic neuritis in children is mainly determined by the results of brain MRI at presentation. They observed that 93% of children with normal MRI remained relapse free. In the ONTT, almost 40 percent of patients had MRI lesions but this trial represents a selected patients group. Small case series of unselected patients have noted a higher coincidence of MRI brain lesions. The yield of spinal cord

imaging is low in unselected patients. Among 115 patients presenting with optic neuritis, MRI abnormalities in the spinal cord were seen in only four patients with a normal brain MRI.

Causes of ON:

The results highlights that the causes namely ADEM and Isolated ON were the major etiology of paediatric optic neuritis. This could be reasoned in the same corollary as explained in the associated factors of disease where in ADEM and Isolated ON were the main cause and was supported by sufficient research results. Further, the research results evidenced that the conversion rate to MS in children was unclear, perhaps due to the variability in study methodologies in published reports and because prospective data was lacking. One pediatric study reported a low conversion rate to MS (4%) (Lana_Peixoto et.al.2001). The risk of MS was estimated to be 13% at 10 years, 19% by 20 years, 22% by 30 years and 26% by 40 years. A different study reported a two –year risk of 36% (Wilejto et.al.2006).

A fourth study reported 16% of their patients with optic neuritis had MS; and children with a prior history of demyelinating disease were not excluded (Brady,1999).

Bonhomme et.al. 2009, 18 patients were followed for more than 24 months and 3 of the 18 (17%) developed MS.

Association between recurrence of causes and the disease incidences:

The results of the association inferred that causes and disease recurrence had significant relationship. The number of occurrences also revealed the etiology of pediatric ON respectively for ADEM, MS, Devics disease with once twice and thrice occurrences. Further the relationship explained the intensity of recurrence and the causes of paediatric ON. One recurrence of paediatric ON was mostly ADEM, twice if occurred was MS and thrice was due to Devics disease. This result is supported by ONTT. Patients who have had an attack of optic neuritis are at a risk of recurrence with at least one documented recurrence in either one or both eyes being 35% in 10 years (ONTT study). This risk was twice as high in those who eventually developed MS (48% vs.24%..$p<0.001$). The final visual outcome remained good despite the recurrences. Good recovery despite a significant axonal los may be due to redundancy in the visual system or cortical plasticity.

This results highlights that a further study is a must to verify that the ADEM, Isolated ON and MS patients further need to be investigated as follow up.

Association between visual acuity and disease occurrence:

The findings of the analysis project that the visual acuity was enhanced following treatment with steroids. Hence visual acuity and disease are independent and not influencing. Hence it is inferred that visual acuity was

free from disease occurrence. This result could be supported by the study results that the treatment enhanced the visual acuity of respondents. It is further explained that disease occurrence had no influence with visual acuity. Most cases of idiopathic or demyelinating optic neuritis have a good visual recovery irrespective of administration of intravenous steroids. Treatment is particularly required in cases with recurrent attacks in patients with a history or evidence of other neurological involvement in atypical cases and in acute optic neuritis in children.

Visual outcome due to treatment:

The results of visual recovery due to treatment revealed a differential pattern over the treatment on different observation intervals like one week, one month and six months. It was inferred that the recovery pattern of visual gain was positive and significantly responsive to the treatment irrespective of the visual ability before treatment.

This result could be explained with the study result of ONTT. The long term visual prognosis of idiopathic optic neuritis remains good. More than 90% of the patients recover a visual acuity of 20/40 or better by 6 months, as seen in the ONTT. A cut off level of vision <_ -20/50(6/15), contrast sensitivity of<1.0 log units and a visual field mean deviation of <_ -15 dB after one month in the ONTT were predictive of a poor visual outcome at 6 months, a prediction that could not be made with any certainty at baseline.

Details of visual outcome due to treatment and optic disc appearance:

The result is inferred that more than half of the sampled number of eyes had temporal pallor due to optic neuritis in children and nearly one third of them had normal vision. This could be explained that despite the relatively good visual outcome, most patients show a degree of long lasting damage to the optic nerve, indicated by a pale optic disc, loss of retinal nerve fibres, prolonged latency in the visual evoked response and thinning of the optic nerve on MRI.

CONCLUSION

Paediatric Optic Neuritis is a rare condition which differs from adult onset optic neuritis in clinical and evaluative aspects. It frequently presents at 7 years of age, more commonly in girls than in boys, usually bilateral, although frequently asymmetric and it is often associated with a febrile illness.

At presentation, children have profound central visual loss, loss of colour vision, a central scotoma, and afferent pupil defect with optic disc swelling and few retinal hemorrhages. Despite the severity of visual loss and optic disc pallor, most children recover good visual acuity. Although it has been established that intravenous methylprednisolone speeds the recovery of optic neuritis, the ultimate effect of intravenous steroids is unknown. Nevertheless, the dramatic recovery shown by patients precludes surgeons to withhold treatment especially in bilaterally affected cases.Though these facts are accepted on a worldwide basis, there are very few series publicised on childhood optic neuritis especially in Indian population.

The present study is undertaken to evaluate the clinical characteristics, neuroimaging findings, efficacy of intravenous steroid, and visual outcome in pediatric optic neuritis with following Aim & objectives:

AIM: Evaluate the clinical profile and assess the visual outcome of Optic Neuritis in Children.

OBJECTIVES:1. To study the clinical presentation of paediatric optic neuritis,2. To assess the visual acuity,3. To identify associated systemic features,4. To study the MRI findings,5. CSFanalysis and 6. To assess the visual outcome after intervention. The study was conducted at the Regional Institute of Ophthalmology and Government Hospital, Egmore by following accidental sampling procedure so as to select 15 respondents with age group of below 18 years old. The inclusion and exclusion criteria were observed and the data were collected as per the schedule and ethical committee's directives. The data were analysed by administering suitable non-parametric statistical tests and the result is summarised as follows.

Age distribution of the respondents was 33% each under the Categories of 0- 5, 5 to 10 and 10-15 years old*.

Females account for 66.67per cent and the remaining of them belong to male

Most of paediatric optic neuritis was bilateral in nature.

Most of the cases in paediatric ON did not express pain on extra ocular movements.

The CSF analysis proved the etiology of ADEM and MS as a cause of optic neuritis in children.

The MRI precisely projects the causes of optic neuritis through more than half of the sampled respondents' brain and spinal cord lesions.

The causes namely ADEM and Isolated ON were the major etiology of paediatric optic neuritis.

The association between the diagnostic causes revealed a significant association between recurrences of the causes and the disease incidence at 10 per cent level of significance in chi-square test. This indicates that even though, there is no recurrence, 40% of the patients had suffered from ADEM and 40% had suffered from Isolated ON and only 10% will not be having symptoms not detectable (NA) and 10 per cent had O.N. The visual acuity and disease were independent and not influencing i.e. visual acuity was free from disease occurrence.

The chi-square value was not significant and hence the associated factors were not influencing the recurrences of the diseases. Both are independent in nature.

The recovery pattern of visual gain was positive and significantly responsive to the treatment irrespective of the visual ability before treatment.

More than half of the sampled number of eyes had temporal pallor due to optic neuritis in children and nearly one third of them had normal vision.

PART - III

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Proforma

NAME :

AGE/SEX :

I.P NO :

CHIEF COMPLAINTS:

DURATION OF COMPLAINTS

PREVIOUS MEDICAL HISTORY : Of similar episode.

PRIOR TREATMENT TAKEN : History of any drug intake or Nutritional deficiency, Iv injections, vaccinations

VISUAL ACUITY AT THE TIME OF EXAMINATION : Snellen's/paediatric picture chart

RE :

LE :

EXAMINATION :

	RE	LE
LIDS :		
CONJUNCTIVA :		
CORNEA :		
PUPIL :		
DIRECT :		
INDIRECT :		

NEAR REFLEX :

SWINGING FLASH LIGHT TEST : To detect RAPD.

IRIS :

ANTERIOR CHAMBER :

LENS :

FUNDUS AND VITREOUS :

TENSION :

INVESTIGATIONS :

Colour vision : with Ishihara Plates.

Fields : With Automated Perimetry

Colour Fundus Photograph

MRI-Brain.

CSF analysis

BLOOD : Tc, Dc, ESR, Mx, Chest x-ray, Blood sugar, X-ray PNS, Hemoglobin,

VDRL, HIV.

Follow up Procedures / Visits: 1 week, 4 weeks and 6 months

No. Of recurrences in the same eye or fellow eye in the follow up period.

Assessments of Parameters : improvement in visual acuity
Improvement in colour vision
Improvement in visual fields
Fundus photography to assess resolution of disc oedema

Age	Gender	A.F	Duration of vision loss	Pain on EOM	PR.Vn	Pupil	Laterality	Fundus	MRI	CSF	Diagnosis	Post Treatment vn					
												1 week	1mnth	6mnths	Fundus	Rec.	
11	f	Fever	1 day	present	RE 1/2 / 60 LE HM+	SRTL RAPD	B/L	Disc edema	H.I Brain	N	ADEM	6\6	6\6	6\6	T.P	-	
9	f	Transverse myelitis	10 days	Absent	RE no PL	RAPD	U/L	Disc edema	H.I spinal cord	N	NMO	6\9	-	6\24	Pallor		3
4	f	-	1 day	-	BE 1/2/60	Ill sus.	B/L	Disc edema	H.I brain& spine	N	ADEM	RE 6\36 LE 6\9	6\18 6\9	6\18 6\9	TT	-	
7	m	Recc.Weakness	1 day	Absent	RE PL plus	RAPD	U/L	Disc edema	H.I brain &spine	N	Recc.Adem	6\60	6\60	2\60	O.A		2
11	f	-	1 day	-	RE 1/2 / 60 LE 6/36	BE ill sus	B/L	Disc edema	N	N	IS O.N	6\6	6\6	6\6	N	-	
12	f	LL numbness	2 days	Present	BE no PL	Ill sus.	B/L	Disc edema	N	OCB	MS	RE 4\60 LE HM	6\36 6\60	6\36 5\60	TP		1
5	f	-	1 day	-	BE HM	Ill sus	B/L	Disc edema	N	N	IS O.N	6\6	6\6	6\6	N	-	
14	m	-	1 day	Present	RE 1/2 / 60 LE HM+	Ill us	B/L	Disc edema	N	N	IS O.N	6\9	6\9	6\9	TP	-	
8	f	Fever	1 day	Absent	LE CF CF	RAPD	U/L	Disc edema	H.I brain& spine	N	ADEM	6\12	6\9	6\9	TP	-	
10	m	-	1 day	Present	BE no PL	Ill sus	B/L	Disc edema	D.M plaque	OCB	MS	RE PL plus LE HM plus	PL 6\60	PL 6\60	O.A TP		3
4	f	Limb weakness	1 day	-	RE PL LE no PL	ill sus ill sus	U/L	RE O.A LE Disc edema	HI spinal	N	NMO	RE PL plus LE 6\18	RE PL LE 6\18	RE PL plus LE 6\18	OA TP		1
3	f	-	1 day	Absent	RE HM	RAPD	U/L	Disc edema	N	N	IS O.N	6\9	6\9	6\9	N	-	
5	m	Fever	1 day	Absent	BE PL plus	BE SRTL	B/L	Disc edema	H.I brain& spine	PR ^	ADEM	RE 6\12 LE 6\9	6\12 6\9	6\12 6\9	TP	-	
6	f	-	2 days	Absent	BE 1/60	ill sus	B/L	Disc edema	Not done	ND	-	6\18	6\18	6\18	TP	-	
15	m	-	2 days	Absent	LE PL	RAPD	U/L	Disc edema	N	N	IS O.N	6\6	6\6	6\6	N	-	

KEY TO MASTER CHART

Age	–	Age in years
Gender	–	M – Male
		F – Female
		Duration of Vision loss in days
A.F	–	Associated systemic features
Pain on EOM	–	Pain on Extra ocular movement
Pr. Vn.	–	Presenting Visual Acuity of the patient
RE	–	Right Eye
LE	–	Left Eye
PL	–	Perception of Light
HM	–	Hand Movements
CFCF	–	Counting Fingers Close to Face
Pupil	–	Pupillary Reaction to light
RAPD	–	Relative afferent pupillary Defect
SRTL	–	Sluggishly Reacting to Light
Ill. Sus.	–	Ill sustained
Laterality of optic neuritis		
U/L	–	Unilateral
B/L	–	Bilateral
O.A.	–	Optic Atrophy
MRI	–	Magnetic Resonance Imaging

H.I	–	Hyperintense lesions
D.M plaque	–	Demyelinating plaques
CSF	–	Cerebrospinal fluid analysis
OCB	–	Oligoclonal bands
ADEM	–	Acute Demyelinating Encephalomyelitis
MS	–	Multiple Sclerosis
Is. ON	–	Isolated Optic Neuritis
NMO	–	Neuromyelitis Optica
TP	–	Temporal Pallor
LL	–	Lower limb